FIVE THINGS THAT WILL CHANGE EVERYTHING

Presented to The National Institutes of Health

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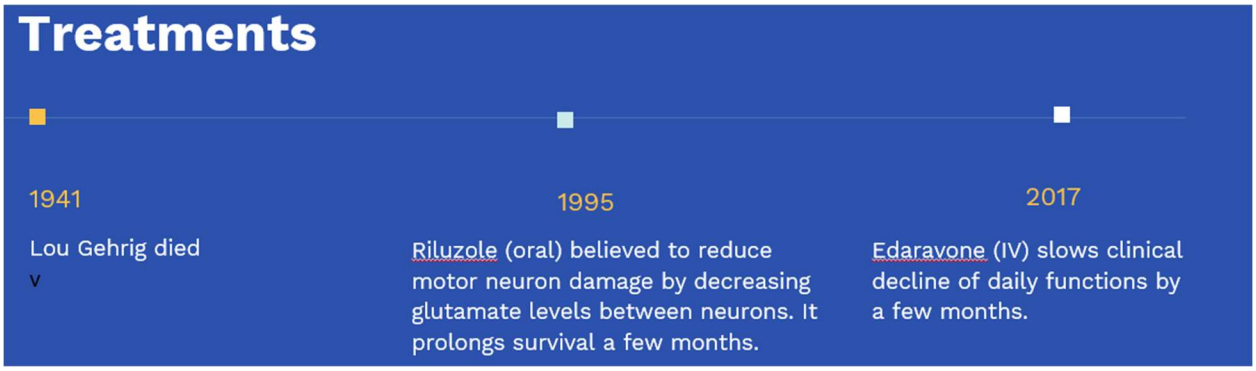
Contents

Abstract

Motivation



Problem

ALS science seems splintered and becomes even more so as the complexity and heterogeneity of the disease becomes more apparent. While the disease progresses quite rapidly, progress on this research is tragically slow. We fail to collect and use data from unsuccessful trials to make the next trials more likely to succeed. We fail to gather the clues that thousands of people with ALS are willing to contribute. Are there ways that NIH can use the expertise and tools that it has delivered for other diseases to help move ALS science forward more efficiently?

Method

A team conducted a search of literature and historical research grant information to find gaps where ALS needs the NIH expertise that has been successful in other disease areas.

Results

We found gaps. ALS lacks a robust, prospective natural history study in the US that can work in tandem with a broad network of clinical trials – both things that NIH delivers well for other diseases. We are also missing infrastructure to enable a productive parallel track. Grants are diverse, disconnected, and relatively small, and the research landscape needs NIH leadership to map out a cohesive roadmap of the science.

Recommendation

Five Things That Will Work Together to Change Everything

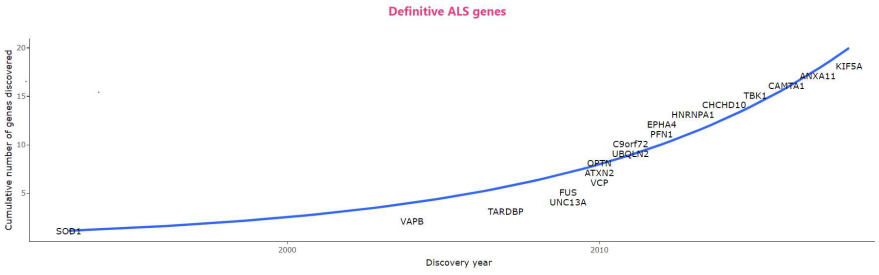
Five Things That Will Change Everything

Where We Are Today

ALS is far more complex than anyone realized even a few years ago.

> "Despite decades of intense research and over 50 potentially causative or disease-modifying genes identified, etiology remains unexplained and treatment options remain limited for the majority of ALS patients."[1]

The ALS landscape is not simple, and it gets less simple with every new discovery. The ALSOD database, developed in Europe, tracks the explosion of gene discoveries implicated in ALS.[2] Few clinical trials outside of gene therapy trials even gather genomics on the participants. Trials continue to fail to meet endpoints, yet some participants are responders, and we're not gathering the genetic data to connect the responder dots. We need your leadership to provide standards and best practices that will give researchers the data needed to better understand who might or might not respond to a therapy and then who actually does and does not respond.



Even this chart of the growth of ALS genes oversimplifies the real world of ALS where polygenetic and epigenetic factors are at play in ALS.

The disease heterogeneity has been the bane of many trials, and we need to flip that into an opportunity to be seized.

Meaningful science is occurring. Discoveries are made every day. A diverse landscape of potential mechanisms and targets are being explored. The NIH RePORTER database shows 653 publicly funded, active projects covering the gamut of mechanisms and stages of research.

In the private and not-for-profit sectors, information seems to be exploding. We are enthusiastic about that. The forward-thinking work that consortia like the Northeast ALS Consortium (NEALS) do keeps pushing the science forward.

Everyone involved knows the urgency that this disease demands. But who is connecting the explosion of information dots?

In recent Congressional testimony,[3] The Biotechnology Innovation Organization said that there are 6,476 clinical development programs in their pipeline, yet only 34 of those are for ALS. They also cited that neurology clinical development programs in general have only a 5.9% success rate, taking approximately 11 years from Phase 1 to approval. We clearly have substantial room for improvement.

There are best practices in other disease areas that have accelerated the results of such research, yet in the ALS world, they are absent. ALS research is fragmented, and data are siloed while people are dying quickly. We don't have a clear, comprehensive map of the research landscape. Nobody is connecting the dots.

One of the NIH goals is to fix problems exactly like this one
"… to expand the knowledge base in medical and associated sciences in order to enhance the Nation's economic well-being and ensure a continued high return on the public investment in research."[4]

The ALS clinical research infrastructure is lacking. We do not reach many people with ALS who would love to participate in a trial. Our trials lack diversity in many ways – racial, ethnic, geographic, age, genetic. A 2017 study showed that 40% of the population lived more than 100 miles away from *any* recruiting ALS interventional trial.[5] A more recent study from IPSOS revealed that financial issues are significant barriers to ALS trial participation, and much of the issue is related to travel expenses.[6] We seem to focus on a small subset of people with ALS who live close to an existing ALS center and who have the means to donate their time and that of their caregiver. The rest are stuck on the sidelines.

In other important ways our trials lack consistency – the consistency of having the right data gathered in the right way. The roadside is littered with failed ALS trials, yet we have not gathered the data that will let us learn from those disappointments. We make the same expensive mistakes over and over. We know of the promise of precision medicine, but most ALS trials are not taking advantage of doing smarter screening, including genotyping. When trials do not hit statistical significance on endpoints, yet still appear to have some positive effect on some participants, sponsors don't have the right data to do smart *post hoc* analyses to inform the next trials.

On Clinicaltrials.gov, there are 452 ALS trials marked as suspended, terminated, completed, or withdrawn. When that set is filtered to those that have results, we only find 90. Less than 20% of trials tell us what happened. The only trials that truly fail are those that fail to teach us anything, and we have far too many of those. We need to normalize failure reporting, just as a smart manufacturer tracks and analyzes data on product weaknesses and failures. We are completely missing any concept of a quality feedback loop in our clinical trials – a building block to any quality scientific method.

The lithium saga reveals one of our big weaknesses. In 2008 a small Italian study showed some efficacy for lithium carbonate in ALS. After everything from do-it-yourself patient observations to more placebo-controlled trials, multiple studies found no positive effect. By 2013 the concept was dead. Then in 2017 some European investigators integrated genetic data with the old lithium trial data, and indeed they found a genetic subgroup that responded. We spent an expensive decade on a scientific roller coaster. We must stop running trials that do not capture the right clues.

"The assumption of a homogenous treatment effect across patients with ALS, for lithium specifically and ALS trials in general, seems no longer tenable and genetic subgroups of patients may modify the treatment effect."[7]

We simply need to work smarter, and that's where the NIH comes in.

The Five Things That Will Change Everything

We lack five things that you have done well in other disease areas. These five cogs will help turn ALS research into a smarter machine running more efficiently and effectively, improving patient and trial outcomes. They fit perfectly with NIH goals[8]:

> The goals of the agency are:
>
> - to foster fundamental creative discoveries, innovative research strategies, and their applications as a basis for ultimately protecting and improving health;
> - to develop, maintain, and renew scientific human and physical resources that will ensure the Nation's capability to prevent disease;
> - to expand the knowledge base in medical and associated sciences in order to enhance the Nation's economic well-being and ensure a continued high return on the public investment in research; and
> - to exemplify and promote the highest level of scientific integrity, public accountability, and social responsibility in the conduct of science.

These five things will not only have an impact on publicly funded ALS research, they will also set standards that can make industry research more productive.

"Natural history study data can serve as the foundation to any therapeutics research program."
Anne Pariser, M.D.[9]

A robust, living natural history study. Today we have a registry at CDC that was designed to do surveillance. It does not supplant the need for a real prospective observational cohort, as exists in cancer and AIDS, in which the progress of disease can be correlated with insights in basic laboratory science and epidemiology.

NIH has led natural history studies that have made significant differences in other disease areas. Clearly they are important since over half of NIH clinical protocols are natural history studies, yet ALS is not yet among the diseases that benefit.[10] We need to change that, especially in such a heterogeneous, rare disease. We need solid, contemporary scientific insights into the disease, its causes, and its

progressions. We need a natural history study run by an agency with the experience and expertise to do natural history studies well and efficiently.

This will finally enable us to

> Identify scientifically based patient subsets based on genetics, biomarker presentation etc.
>
> Reduce reliance on mouse and zebrafish pre-clinical research in favor of a representative group of patient IPSC stem cell lines
>
> Enable *post hoc* clinical trial analyses of why therapies work for some but not all people with ALS. What is different and distinct about responders that has a scientific basis?
>
> Provide a tissue repository with robust associated patient data.

Government is good at establishing data standards for pertinent data points and at collecting data. We need to leverage that and start collecting the dots in a smart and well-planned manner so that scientists can connect the dots. This will be the basis for everything we do in our Five Things That Will Change Everything.

We know that a NIH natural history study will be done right, and in harmony with "FDA Guidance on Natural History Studies."[11]

Electronic health records, especially those from ALS clinics, may be helpful in populating this study, and there may also be a complementary benefit of data standards enhancing the measurements and data collection taken at clinics.[12]

ALS has some natural history studies that were funded largely with donor funds. Such studies as Answer ALS have provided a depth of helpful data, but the limited patient numbers are also limiting on how much can be discovered using them. We need a deep and broad study. We need lots of data, and people with the ticking ALS clock need the discoveries that a broad base of data will spark. Now.

"AMP PD is a true example of the whole being greater than the sum of its parts," said Walter Koroshetz, MD, director, National Institute of Neurological Disorders and Stroke (NINDS).[13]

ALS, like PD, needs a whole that is greater than the sum of its parts. ALS needs both a prospective cohort study collecting clinical, laboratory, quality of life, and epidemiological data and a retrospective cohort study collecting clinical, laboratory, quality of life, epidemiological data.

If a natural history is a foundation to propel science, every person with ALS deserves a chance to participate.

"Our experience raised several equity issues around how we grapple with diseases like ALS when treatments are scarce and where most patients, like Rahul, who screen for clinical trials, are not enrolled."
Maya Vijayaraghavan, MD, MAS[14]

A comprehensive network of clinical trials that reaches more people (who are eager for trials, by the way) and that accelerates more broad research. This is akin to the clinical trials networks for cancer and AIDS—widely dispersed across the US to ensure accessibility to more patients and with the ability to do efficacy studies, sophisticated sub-studies on pharmacology, immunology, genetics, quality of life, etc. We need to smarten up inclusion criteria and measures we collect so that trials always inform the next trials. We can't afford to keep doing trials where accountants influence the data that they collect solely on the cost per data element per patient. Science needs to lead these decisions.

In the recent House Energy Committee Health Subcommittee hearing on Neurodegenerative Diseases, we heard about the importance that NIH puts on trial access and diversity. We heard that NIH even had resources to pay to get people to the NIH for trials. Our enthusiasm was tempered by the reality that there are just three recruiting ALS clinical studies at the NIH Clinical Center, only one of which is interventional.[15]

There are just three other recruiting NIH-funded ALS interventional trials at other sites listed at clinicaltrials.gov.[16]

The National Cancer Institute has a network that supplies clinical trials at over 2200 sites.[17] The HEALEY Platform trial (funded by generous philanthropy) which is the paragon of accessibility and trial design for ALS is available at only 51 sites in 28 states. Other ALS trials fall well short of that.

There is true enthusiasm among many with ALS to participate in a clinical trial. It's their only shot at something, and it's an important contribution to advancing ALS science that many people facing their own mortality are glad to make. The IPSOS poll[18] shows some of the barriers to participation such as travel expense, inability to travel, and exclusion criteria. We need to remember that man-made barriers merely require man-made solutions, and nobody is better at those solutions than the NIH.

"The majority of patients with ALS are excluded from trial participation, which questions the generalizability of trial results."[19]

There simply aren't enough seats on the clinical trial bus today (at most 3000 seats per a recent manual count by a member of this team), and the bus doesn't travel to very many places. People in major cities like Buffalo and Indianapolis seldom have access to trials, and access is even worse for the thousands with ALS who are not in urban areas. There is a current social media campaign that is quite successful -- #ALSisEverywhere . Unfortunately, ALS clinical trials are not to the approximately 27,000 people with ALS who can't get a seat on the bus.

We need more trials in a network that is designed to measure the right things in the right people at the right times. Again, these are things that NIH does well for other diseases. People living with ALS also deserve your expertise.

Many ALS trials are sponsored by thinly capitalized companies with no revenue or earnings. Robust data gathering and smart *post hoc* analyses to inform the next trial are viewed as luxuries.

Even our outstanding HEALEY Platform trial, while far more inclusive than many trials, is not accessible by location or by inclusion criteria to many. Because it is privately funded, its ability to grow and be more inclusive of people with ALS is limited.

Many of today's ALS trials are gathering interesting potential biomarker information in their silos, but nothing is close to the level of being an accepted surrogate endpoint. We are doing interesting science experiments, but the body of work is not designed in a collaborative manner to support the end-goal of a sound surrogate endpoint.

ALS also will benefit from standardization of data definitions and clinical research protocols. Who knew there were so many ways to do a lumbar puncture? People with ALS know. And we can't afford to confound trials because of a lack of good protocols.

A solid natural history Study will also draw collaboration with standards and valuable shared data. It is also an opportunity to reach out to underrepresented communities to make sure we include them in a core study that will become a building block for much ALS research.

Think about how two of our cogs, the natural history study and a clinical trial network, can work together. Trial selection can be more precise. Trial measurement can be more complete. Trial analysis will be smarter because of a more complete picture of each participant being gathered. And since we so often see trials fail to meet primary endpoints but at the same time observe people in trials who report benefit, we will finally have the scientific data to analyze and identify responders' characteristics in order to inform the next trial.

"EAPS can be designed to also learn about ALS. For example, in one of our EAPs, we learned about how to best dose the medication using biomarkers. In another, we found that breathing function improved in several of the participants."
Merit Cudkowicz, MD, MSc [20]

A framework for broader insights into the disease while maintaining the scientific rigor of narrow randomized controlled trials (RCTs) – a parallel track. Stringent efficacy data from our RCTs can be complemented with effectiveness information from broader programs. We miss opportunities today because we lack any infrastructure to allow real-world evidence to complement that rigorous clinical trial data. Enable the use of the Expanded Access path that large pharma companies quietly use today in oncology to gather informative data on larger populations and at the same time provide access to people who cannot get into trials. This idea—a novel one for many—creates a common platform for access to trials for those who may not fit the eligibility criteria for efficacy studies for new drugs. It also offers the chance for studying individuals who represent a broader cross-section of people living with ALS and offers wider generalizability and greater external validity than the more narrowly defined phase 2 or 3 clinical trial. A common platform for this purpose can collect clinical endpoints, severe adverse events at a minimum (again done in AIDS for drugs like ddi and d4t in the "parallel track") or can stand as a hybrid mechanism, part clinical trial/part natural history cohort, collecting more laboratory and clinical data on people living with ALS, whether or not at any given moment they are receiving an investigational drug. Today, those with ALS who cannot get into a trial have scant opportunities for Expanded Access.

If natural history study participants find themselves ineligible for trials, we can still track meaningful data about their ALS by enabling data collection in an Expanded Access, parallel track framework.

By providing a framework to enable informative data gathering, NIH can create a usable path for many small companies that will gather data in a meaningful and shareable way.

There is precedent for this in the NIH-funded work at the University of Michigan on TEAMSS - Transforming Expanded Access to Maximize Support & Study[21]

Now envision the first three cogs working together, each helping the others. A person with ALS signs up for the natural history study, and it becomes apparent that the person does not qualify for a current clinical trial. No time is wasted finding an Expanded Access Program (EAP) that will not only be welcomed by the patient but also be informative to the science with the natural history data that can complement the evidence gathered during the EAP.

''ALS research could certainly use the kind of leadership from the NIH that has been so productive for cancer and infectious disease research. As a family member who has been affected by the devastation of ALS, we need the NIH and its expertise and infrastructure to help end ALS."
Senator Lisa Murkowski

NINDS leadership. Your leadership will be huge for us.

In 2020, the NIH invested $107 million in ALS.[22]

The table below shows a few details:

NIH ALS Spending 2020	
Total NIH	**$107,076,085**
Average	$440,642
Number of Entries	243
Maximum	$4,807,854
Minimum	$22,866
Number greater than $1,000,000	15
Number less than $100,000	52
Total NINDS	**$54,249,306**
Total NIA	**$44,356,659**

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While there are some large grants in ALS research, the vast majority (almost 80%) are under $100,000, which allows for only small studies, underpowered and uncontrolled, noted in the field for years.[23] We can and will work to increase NINDS budget for ALS research, but right now we are asking you to conduct an outside review of the NIH's entire portfolio on ALS (again, as was done with AIDS in the Levine report) to insure the disparate efforts across the NIH Institute/Centers (ICs) have not created redundancies and gaps in our work. Please be the leaders to connect the dots and to find and acknowledge the gaps where we are missing research opportunities.

Along with our emphasis on natural history and clinical trials, we also realize the critical importance of the diverse early science that must happen in order to unravel the mysteries of ALS. We believe that your NIH leadership of the basic science that will eventually lead and feed the clinical pipeline is crucial to finding treatments sooner.

We not only need to identify redundancies and gaps, but we also need to be aware of research opportunities that could provide far-reaching efficiencies. Cold Spring Harbor Labs has received support from NIH via NINDS and NIA as well as from charities and foundations for its work that has identified

three molecular subtypes of ALS.[24] Remarkably, every patient whose brain tissue they have studied fits into one and only one of the three subtypes. This kind of work, started with the help of NIH could have profound effects on clinical trial design and identification of likely responders (an area where ALS trials have been disappointing in the past). Are we seizing the opportunities for continuing this research that could have a ripple effect throughout ALS clinical research? We need your leadership to make sure that this kind of work does not die on the vine. We need your leadership to help projects such as this find synergistic partner projects so that they move forward more quickly.

We have been inspired by the European Neuronet[25] platform – a kind of air-traffic control center for their diverse research on neurodegenerative diseases.

Please be the leaders to find the gaps and the opportunities in our ALS research landscape and help us connect the dots.

"It will take compassionate leadership from NIH, unwavering support from Congress, innovation from Trial Sponsors, and brilliance from top neurologists and scientists to move our disease forward. We are willing to fiercely pursue all of this until our very last breath."
Sandy Morris, Person Living With ALS

Our relationship. AIDS activists have had an ongoing 30+ year relationship with Dr. Fauci at NIAID, with a series of NIH directors and directors of other ICs, like NIMH and NIDA. People living with ALS need to be in your inner circle too. This means we hope this is our first, not our last meeting with you and we can talk regularly on a variety of strategic and tactical working teams. We also would like you to put a person living with ALS on the NINDS Council. We realize that this may create issues of fairness with other diseases and see rotating patient representation between ALS, Alzheimer's, and other neurodegenerative diseases over a series of years as a way forward in this regard.

Our team is thoughtful and motivated. There are many more in the wings. As you know, ALS steals some of our best and brightest. Put them to work. We can change everything together.

Everything Works Together

These five things that will change everything are not independent. They are cogs in a machine that must work together for optimum results. The last thing we want is to build more silos.

Think about the powerful possibilities of this efficient machine.

Imagine if a person with ALS signed up for a NIH natural history study and immediately clinical trials could screen (with better scientific criteria than are used today) and enroll her or him, taking advantage of the data that had already been gathered the right way by the NIH.

Imagine how much faster we could screen for trials, a process that has been historically slow and inefficient for ALS.

Imagine how inhumane run-in periods for trials could be reduced or eliminated using sound natural history data.

Imagine if a person with ALS who was diagnosed long after onset (thus ineligible for a trial) and was in the natural history study opted into a large EAP that ran in parallel with a trial.

Imagine one-stop shopping for terminal patients. People with ALS could access a clinical trial or EAP closer to home and participate in a natural history study in the same visit.

Imagine the insights we could discover that are absolutely lost today.

Next Steps -- Action Items

- **NIH commitment to the five solutions**
- **NIH teaming with ALS Problem Solvers to advance the solutions**
    - **A person with ALS on the NINDS Council**
    - **Forum for regular, purposeful interaction between NIH and Problem Solvers**
    - **Assignment of leadership team, action teams with businesslike project management**
    - **Integration of our recommendations into current budget discussions**
    - **Target dates and project plans**
    - **Next meeting date**

Why NINDS

You know how to do all five of these things, and you do them well.

NINDS has the scientific expertise.

We need for you to use the solutions NIH has delivered in the past to advance other disease areas and apply them to ALS.

The ecosystem for ALS research is clearly out of kilter today. The mission of NINDS is to seek fundamental knowledge about the brain and nervous system and to use that knowledge to reduce the burden of neurological disease for all people. These five cogs fit your mission hand-in-glove. We need you.

There is too much work going on in ALS research to allow it not being done in the smartest and most efficient ecosystem. In the past, ALS research has benefited from your extramural grants. We also need your intramural research and your collective knowledge. We need agile and efficient project management at the most basic level.

You have delivered groundbreaking solutions with great success in other disease areas. We ask you to apply these same proven protocols to ALS science. You will change everything for those suffering with this tragically underrepresented disease. This is the commitment that we ask and that people with ALS deserve.

Together we will change everything.

Thank you.

Danielle Boyce

Mary Catherine Collet

Merit Cudkowicz

Gregg Gonsalves

Philip Green

Robert Hebron

Timothy Lowrey

Sandy Morris

Becky Mourey

Gwen Petersen

Glen Rouse

Other Supporters

Our Team (and Your Team)

Danielle Boyce

Danielle Boyce is an advocate, researcher, public speaker, and writer in the neurology space. Her work has appeared in dozens of scientific journals and her children's book, *Charlie's Teacher*, is used in children's hospitals throughout the country. She has served on several patient and caregiver advisory panels for academic institutions, pharmaceutical companies, nonprofits, the Food and Drug Administration, and PCORI. She has a master's in public health with a concentration in epidemiology and recently completed the requirements of the doctorate of public administration. She currently volunteers for I AM ALS and Answer ALS.

Mary Catherine Collet

Cathy Collet's career has led her down some paths that have also informed her approach to patient advocacy. After working for Eli Lilly and Company for 18 years, she became one of the founders of a small consulting practice specializing in benchmarking studies. She recently retired from that role after 23 years. Cathy's degrees are from Saint Mary's College (BS. Math) and from the University of Notre Dame (MS. Math). When her mom died from ALS in 1997, she thought that it was outrageous that the prognosis was the same that Lou and Eleanor Gehrig faced in 1939. Her passion is to improve public policy and clinical research to change that prognosis for others. Cathy volunteers for and supports multiple ALS organizations. She has been a Stanford University MedX e-patient scholar. She is one of the founders of www.MoreThanOurStories.org and is on the selection committee for the ALS MND Symposium Patient Fellows Program. Cathy is a Fellow of the GE2P2 Foundation. She received the Amazing Advocate Award from the ALS Association Indiana Chapter and participated in the ALSA national advocacy day for 16 consecutive years. She was recently honored with the Humanitas Award from Saint Mary's College for her ALS advocacy work.

Merit Cudkowicz

Neurologist | Clinical Researcher
Chief, Neurology Department
Director, Sean M. Healey & AMG Center for ALS
Julieanne Dorn Professor of Neurology, Harvard Medical School

Gregg Gonsalves

Gregg is Associate Professor of Epidemiology (Microbial Diseases); Affiliated Faculty, Program in Addiction Medicine; Associate (Adjunct) Professor of Law, Yale Law School; Co-Director, Global Health Justice Partnership; Co-Director, Collaboration for Research Integrity and Transparency at Yale University. He is also our inspiration.

Philip Green

Since his diagnosis with ALS, Phil has made his life's work improving the fight against this disease. He is active with many patient advocacy organizations and serves as a volunteer patient advisor to several companies working on ALS therapies and technologies. His involvement includes:

Augie's Quest, Leadership Council, Team Gleason, Board of Directors, International Alliance of ALS/MND Associations, PCAC (PALS & CALS Advisory Council), International Alliance of ALS/MND Associations, Innovation and Technology Council, ALS Association, PCAC (PALS & CALS Advisory Council), Cytokinetics, Patient Advisory Board, Clara Health, Breakthrough Crew, MT Pharma, Technology Advisory Board, HEALEY Platform Trial, Patient Advisory Committee, HEALEY Platform Trial, Recruitment and Retention Committee, UW Medicine Center for Translational Muscle Research, Patient Advisor , CDMRP ALS Research Program, Consumer Reviewer, I AM ALS, Clinical Trials Committee Co-chair, I AM ALS, Legislative Affairs Committee, I AM ALS, Community Advisory Committee, NEALS, Research Ambassador, International Symposium on ALS/MND, Patient Fellow (2019, 2020)

Robert Hebron

Bob earned his BA in economics from Columbia College 1976 and his JD from Fordham University Law School 1979. He had a 28-year career at New York Life as Chief Insurance Counsel and later a Senior Vice President managing a large business unit that included its own actuarial area, pricing, selling, and managing life insurance products. Bob was Chair of the Hope Now for ALS movement. In addition, he served on the patient/caregiver subcommittee for the ALS Association FDA guidance document development project. Bob's daughter, Beth, is living with ALS. She is just 33 and was diagnosed almost 8 years ago.

Timothy Lowrey

Tim has been a licensed pharmacist for almost three decades after having graduated with honors from The University of Florida in 1992. He spent most of his career in retail pharmacy at Publix and Wegmans and enjoyed helping patients improve their health and well-being. He feels lucky to have traveled the world, volunteered to renovate houses for members of his community, grown an organic garden of healthy and tasty vegetables every year with enough to give away, built furniture, read a book every week for years, ran pretty much daily and have had three dogs, all rescues. He shares his life with his wife of 16 years and best friend, Emily, who left her own hard-earned career to spend precious time with Tim.

Tim was diagnosed with ALS in October of 2018. ALS is taking his physical abilities away His wife says my positive attitude is one of her favorite things about Tim, and ALS will not take that. It won't take his passion to advocate for advances in treatments for ALS either. He knows it is likely to be too late for him, but he doesn't want to pass this on to the next generation. He has been an advocate for people with ALS since the summer of 2019, when he started raising money for Team Gleason and has been with I Am ALS over the past year. He will be an advocate for the rest of his life.

After seeking experimental treatments through clinical trials, Tim saw and lived through a process that needs vast improvement on access, information, and direction. Volunteering for the I AM ALS clinical trials team has allowed him to work on these issues. After applying to various trials at four locations, Tim was finally accepted into one 360 miles from home. Tim is also part of the I AM ALS Community

Outreach team educating healthcare students at various schools and institutions around the country on living with, and caring for patients with ALS.

Throughout his professional career Tim has needed and depended on federal agencies like the FDA and CDC for trusted guidance, safety, and leadership. Today, he asks for NINDS to be the leader to get us the 5 things we need to advance ALS research and make it a manageable disease.

Tim earned his Pharm D degree from the University of Florida College of Pharmacy. He is a licensed pharmacist in Florida, New York, and Alabama. He holds multiple APhA certifications. He has been a pharmacy intern preceptor for the University of Florida, SUNY at Buffalo, and Samford University.

Tim is a member of the ALS Association Buffalo, NY Chapter.

Sandy Morris

Sandy lives near Lake Tahoe, CA with her husband of 31 years and their three amazing children ages 23, 21 and 19. She worked for Hewlett-Packard for almost 30 years, managing multiple international teams for the consulting area. Her last job was in global business analytics.

Sandy lived an active lifestyle. She suffered no health issues in her lifetime and feel incredibly blessed for the life she had been allowed to live. She was diagnosed with ALS on January 6, 2018, at the age of 51 years old. Her symptoms started with right foot drop; so subtle she didn't put much thought into it, until the progression continued, and she was barely walking.

Sandy was thrilled to be a participant in the Brainstorm NurOwn stem cell Phase III trial. There were tight eligibility criteria and she felt grateful to be a part of advancing science. Her family has traveled with her to South Korea four times for Corestem where she received three bone marrow aspirations, three spinal infusions and four lumbar punctures at her own cost. She was recently in the Brainstorm EAP where she was lucky enough to receive three more spinal infusions.

Sandy became a fierce ALS advocate after her trial experience and vowed to make changes in this destructive disease. She partnered with Brian Wallach, founder of I Am ALS, in 2018 to lead the Patient Advisory Council and Clinical Trials Team. Standing on the shoulders of giants, we worked with the FDA leaders to get the guidance document for clinical trials updated in September 2019. They met with over 30 ALS drug sponsors to introduce the Patient centric trial design (PaCTD) ratings. They created an ALS Caucus which currently has over 150 members. Recently they have been involved with getting over 310 co-sponsors for the bill H.R.3537/S.1813 Accelerating Access to Critical Therapies for ALS Act (ACT) which insures expanded access programs, as well as establishing a Consortium at the FDA level.

Sandy has degrees in Business Administration and Communication from California State University, Sacramento, where she also earned an MBA degree.

Her ALS organization involvement includes I Am ALS Lead for Community Advisory Council - 2018-2020, I Am ALS Lead for Clinical Team-2018-2020 Co-lead 2021, Healey Platform Trial Patient Advisory Council, Healey Platform Recruitment & Retention Team, Prosetin Community Advisory Council, Amylyx Advisory Council. She has been honored with the ALS TDI Stephen Heywood Award 2020, Healey Center Inspiration Award 2021, Unite's 2020 ALS Community Advocate Award Runner Up.

Sandy was a speaker at NEALS Annual Meeting-Expanded Access - September 30, 2020, a panelist for Duke Margolis/FDA Project - January 27, 2021, and a patient speaker at ALSA FDA meeting - May 25, 2021. She is a member of her ALSA local chapter in Sacramento, California.

Becky Mourey

Becky has been living with ALS since November, 2020. She is an accomplished musician with a Bachelor of Music degree from the Hartt School of Music. She has over 20 years of experience as a private clarinet and saxophone teacher and has performed with the Wellesley Symphony Orchestra and the Claflin Hill Summer Winds. She also has experience in the insurance industry. Since her diagnosis she has become involved with the I Am ALS Clinical Trials Team as well as their Legislative Affairs Team. She leads her own weekly ALS advocacy group and has organized a walk for ALS ONE. She was a Congressional meetings panel member for the ALS Association's 2021 Advocacy Day. She was honored to represent the ALS Association Massachusetts Chapter on the field at Fenway for the first Lou Gehrig Day. Becky is a volunteer member of the Patient Advisory Committee at Sanofi Genzyme.

Gwen Petersen

Since her diagnosis with ALS at age 32, Gwen Petersen has poured her energy into advancing the science of her disease. Gwen has participated in more than thirty-five observational ALS studies, 10 of which are ongoing, as well as two interventional trials with an experimental therapy. Prior to her diagnosis, Gwen worked as a Recruiter for one of the top ten medical centers in the country.

Her accomplishments include:

> The New York Times, *As M.L.B Honors Lou Gehrig, It Shines a Spotlight on A.L.S*, published June 2, 2021, CBS SF Bay Area (KPIX) news segment, *A Dosage of Hope*, aired August 10, 2021, Selected as Patient Fellow (1 of 6 global selections) for 2019 ALS/MND International Symposium- world's largest conference on ALS/MND, Selected as Research Ambassador for 2018 Northeast Amyotrophic Lateral Sclerosis Consortium (NEALS), Clearwater Beach, FL, October 4-5, 2019, CDMRP ALS Research Program, Consumer Reviewer, FY2020 & FY2021, Patient Advisor to Pharma: Alector, Amylyx, Annexon, Apellis, Corcept, Cytokinetics, Denali, Healey Center ALS Platform Trial, Healey Center ALS Expanded Access Programs, Orion, Orphazyme, PatientsLikeMe, Project ALS, Sanofi, Seelos, Verge Genomics

Glen Rouse

Glen was diagnosed with ALS in September, 2020. He's a member of the I AM ALS Clinic Trials and Legislative Affairs Teams. He also enrolled in the HEALEY Platform trial in the regimen B arm. Glen has recently joined Cytokinetics' ALS Patient and Caregiver Advisory Council (ALS-PAC).

Since 1992 he has worked as an Inventory Forester for Sierra Pacific Industries, a large timberland company which owns over 2.1 million acres of sustainably managed timberland in California and Washington state. Most of his job involves performing GIS analysis and data manipulation. Glen is the software development forester charged with design and development of field technology programs that crewmembers use to collect data in the woods. He is also the project forester for SPI's Giant Sequoia Genetic Conservation program, which involves collecting cones from the approximately 67 natural

groves, extracting seed, growing seedlings which are then out planted to establish new groves at more northerly latitudes as a hedge against catastrophic wildfire and climate change.

Glen earned a B.S. degree in Forest Management from Humboldt State University, 1991, and he is a California Registered Professional Forester (# 2552).

We are grateful for the guidance and support provided by

Barbara Kipp who is a retired partner with PricewaterhouseCoopers, and an industry leader in Business Ethics. Bobby is also an amateur musician, and strong supporter of her good friend, and ALS patient, Becky Mourey.

Carol Louik who is another supporter of her good friend Becky Mourey and has a doctoral degree from the Harvard School of Public Health. She has worked as an epidemiologist and faculty member at Boston University.

Alison Bateman-House
Assistant Professor, Department of Population Health
NYU Grossman School of Medicine

Lisa Murkowski
United States Senator
Alaska

We Work in Accordance with The Morris ALS Principles

ALS, a devastating neurodegenerative disease discovered in the middle of the 19th century, has killed millions of people across the globe. Yet more than 150 years later, there are no cures, no effective treatments, no urgency. This is unacceptable.

Today, we unite as leaders to end ALS. We take ownership of our disease so that the road to cures is faster, equitable and more humane. We are not *subjects* or *victims,* and are only occasionally *patients*, a term which implies passivity. We are a relentless community working alongside researchers, policymakers, and clinicians to identify and cure this heterogeneous disease. We demand a seat at the table *before* decisions are made in drug trial design, research, healthcare policy or anything that affects our care. From this point forward, we will not tolerate siloes, disorganization or lack of urgency by any agency or organization that serves us. There will be *Nothing About Us Without Us.*

We live on the ALS Clock. * ALS is stunningly brutal and kills us quickly. Our political leaders must make ALS research and therapy development a national priority. Our nation has rallied to confront HIV/AIDS, cancers, multiple sclerosis and now COVID-19. We demand that the United States leaders make a commitment to end ALS.

We will:

1. **Protect** our intellectual, physical, and financial dignity.
2. **Be global stewards** of our disease and respected partners in the science of treatments and cures.
3. **Act as trusted peers** with clinicians, researchers, and policymakers.
4. **Fight** for equity in decision-making.
5. **Lead** to end ALS.

This impacts you!

Healthcare professionals

- Communicate with us and about us as though we are *living* with ALS. We are partners with you in our own care.
- Encourage every Person Living with ALS to consider clinical research by providing timely, comprehensive information about approved and investigational therapies. We are experts in our own disease and deserve to be informed.
- Provide accessible clinical and research options, including telehealth.
- Give options for genetic counseling and testing, even for those with no known family history of ALS.

Scientific community & ALS research community

- Provide virtual and in-person access to all ALS/MND conferences and scientific meetings for People Living with ALS.
- Include People Living with ALS on all clinical trial protocol teams, on advisory bodies to the National Institutes of Health, the Food & Drug Administration, Centers for Disease Control & Prevention.
- Build Expanded Access Programs (EAPs) into drug development plans. EAPs for other diseases were key routes to extend experimental therapies to those not eligible for trials and to learn more about the therapies and the disease. Sponsors must design trials that adhere to the Patient-Centric Trial Design (PaCTD) rating criteria.
- Share your data, designs, failures, and best practices. Your duplication of work is deadly.

ALS policy community, legislators & regulators

- Prioritize finding treatments and cures as if your loved one was living with ALS. You must move as aggressively as the disease itself.
- Execute *real* pathways to access experimental treatments through EAPs or a national ALS clinical trials network.
- Mandate a reliable census of People Living with ALS with an annual report that uses modern technology and information science as the current epidemiology in the US is poorly understood.
- Create policies that provide coverage for care and caregivers.
- Treat ALS as the non-partisan issue that it is.

ALS nonprofits

- Amplify and serve the diverse People Living with ALS.
- Focus on your core competencies and celebrate the successful efforts & results across the Community. Work together to address the critical gaps that are preventing real progress.
- Don't treat us as mere fundraising opportunities for your organization. We are the people you serve and must be involved in every facet of operations, including your board of directors.

*** The ALS Clock**

This disease will kill 50% of us within 3 years, it will kill 90% of us within 5 years.

Our lives are worth saving. Work with ***that*** kind of urgency.

This document was created by those living with and impacted by ALS.

ALSPR1

4/30/2021

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