



# GLOBAL RESEARCH PROGRAM

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ASSOCIATION

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October 10, 2017

Hello,

We hope you enjoy this detailed look out our global research program. We have the premier ALS research program in the world, led by the premier ALS scientist in the world, Dr. Lucie Buijn. We are the largest private funder of ALS research in the world and thanks to the ALS Ice Bucket Challenge, we are spending three times as much on ALS research as we were before the summer of 2014. Since our research program was founded in 1985, our focus has led to significant ALS research breakthroughs.

Our approach is simple: we fund the best, most promising research anywhere in the world. This approach has led to some of the biggest research discoveries in the history of ALS. We also inspire and initiate innovative partnerships across all sectors – government, industry, academia, and other non-profit organizations. Thanks to our donors, we are currently funding nine global collaborations.

Research is a critical part of our mission. We are also the leading organization providing care services for people living with ALS around the country, as well as advocating for increased funding for ALS research and improved public policies. Everything we do supports our mission of finding treatments and a cure for ALS.

If you'd like to learn more about our global research program, including what specific research projects and/or clinical trials are occurring in your area, please visit our website at [alsa.org/research](http://alsa.org/research).

Thank you for your interest and support. We are committed to creating a world without ALS.

Sincerely,



Barbara Newhouse  
President and CEO  
The ALS Association



OUR VISION: Create a world without ALS.

OUR MISSION: To discover treatments and a cure for ALS, and to serve, advocate for, and empower people affected by ALS to live their lives to the fullest.

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**SECTION 1:  
OUR RESEARCH STORY**

# RESEARCH

## TREAT ALS™ Global Research Program Narrative

### SUMMARY

The ALS Association's global research program has remained at the forefront of ALS research since its inception in 1985. We are the largest private funder of ALS research worldwide, and our efforts have led to some of the most promising and significant advances in ALS research. Our approach is global – the world is our lab – enabling us to fund the top ALS researchers worldwide and ensure that the most promising research continues to be supported. We fund projects across the research pipeline, from basic research through clinical trials, and our support has led to several potential treatments currently in clinical trials. Since the ALS Ice Bucket Challenge in 2014, we have tripled the amount we spend in research every year – from \$6 million to over \$18 million – and we are committed to maintaining – and even increasing – this level.

***We are the largest private funder of  
ALS research worldwide.***



### OUR HISTORY

Since its inception in 1985, The ALS Association's global research program has led the way on ALS research. The program was established by Robert Abendroth, one of the founders of The ALS Association and long-standing member of the Board of Trustees. The program was originally modeled after a National Institutes of Health (NIH)-style program that funded basic research grants. When The ALS Association decided to expand our research funding, Mr. Abendroth invited Dr. Tom Maniatis, a world renowned geneticist and molecular biologist, to lead and assemble an advisory board of experts to help identify critical gaps in ALS research. In 2001, they recruited Dr. Lucie Buijn, to run the global research program and to expand our grant portfolio to include translational research studies, our postdoctoral fellowship, and clinical trial programs. As the program expanded, it was renamed Translational Research Advancing Therapies for ALS, or TREAT ALS™.

Today, Dr. Buijn serves as the Chief Scientist of The ALS Association and continues to build programs to support The ALS Association's research goals. She is recognized as an international leader in the field and represents The ALS Association on several scientific and research committees worldwide. Dr. Buijn and ALS Association Executive Vice President of Strategy Calaneet Balas direct the TREAT ALS™ global research program with guidance from The ALS Association's Research Committee.

## OUR APPROACH TO RESEARCH

Through TREAT ALS™ we are dedicated to a collaborative and global approach. Since our inception, we continue to accomplish significant advances in ALS research. Everything we do works toward discovering ALS treatments and a cure. We do not fund one laboratory, but instead take a global approach in funding the most promising researchers worldwide, whose projects span the entire research pipeline. This covers a wide breadth of scientific focus areas – each is critical to advancing research – while spurring innovation along the way.

Collaboration is the cornerstone of our research program. Rather than conducting research in our own proprietary laboratory, our unique approach to advancing ALS research involves forging partnerships among academic institutions, industry (pharmaceuticals and biotech firms), government, and other nonprofit organizations. We host yearly scientific workshops and symposia to bring the foremost ALS experts together to discuss and explore various ALS research topics, leading to the generation of novel research ideas.

We also focus on the future of ALS research by supporting and attracting bright, young scientists to the ALS field. We foster their creative ideas and hard work to incite advances and propel them to the next level to start their own ALS research laboratories.

*Everything we do works toward discovering ALS treatments and a cure.*

## HOW WE WORK

Through TREAT ALS™, we maintain a large grant portfolio. All studies funded through the organization undergo competitive review. Every year, we receive hundreds of grant applications, and the number of applications received has doubled since the ALS Ice Bucket Challenge. Leading experts in ALS and related fields from around the world review our grant program to select the most promising ALS projects. Our grant review process is rigorous, following policies and procedures that are in place to maintain the utmost integrity of the research program. Members of our Research Committee provide oversight for final approval of the grants, and the Board of Trustees gives the final approval.

## OUR ACHIEVEMENTS

To date, The ALS Association has funded more than \$150 million in ALS research. Currently, we are funding over 126 active research projects in eight countries, all selected through our competitive peer review process, involving top ALS scientists. We are the largest private funder of ALS research worldwide. Our unrelenting focus has resulted in some of the greatest ALS research discoveries in history. From the earliest stages of our program, The ALS Association has recognized novel approaches that have led to significant ALS research breakthroughs.

## EXAMPLE OF OUR TRACK RECORD OF SUCCESS

The ALS Association has a strong track record of success when it comes to advancing research. The ALS Association was the first to invest in antisense technology targeting the second most common genetic cause of ALS: SOD1. We supported antisense research despite the high risk of the technology not coming to fruition. Our initial investment of \$1.5 million to ALS researchers propelled the concept all the way from an academic laboratory in partnership with industry to testing the approach in the clinic. Currently, a clinical trial for people carrying the SOD1 mutation is ongoing, with plans to begin a clinical trial targeting C9orf72, the most common genetic cause of ALS, in the near future.

Our translational approach facilitates the development of potential antisense treatments not only for ALS, but also for other neurodegenerative diseases. In this way, the value of our initial investment has ballooned from \$1.5 million to more than \$100 million. In December 2016, the FDA approved antisense technology targeting spinal muscular atrophy, a common neuromuscular disease, which is the leading genetic cause of death in infants and toddlers. This is the first approved treatment for this fatal disorder. This success gives us much hope for the future of antisense therapies targeting ALS.

## THE FUTURE

Building on success, our research program continues to evolve with an increased focus on people living with the disease. Driven by a sense of urgency, we are driving drug development while leveraging innovative partnerships with industry, the investment community, and federal agencies. In the years ahead, we will see an increase in the number of clinical trials, as many of the newer approaches in gene therapy continue to expand. Through engagement with the Federal Drug Administration (FDA) and the voice of people living with the ALS, clinical trial design and biomarker programs will be enhanced.

We are in an era of precision medicine that targets an individual patient's disease process and takes into account individual variability in genes, environment, and lifestyle. As a result, many more large collaborative partnerships will emerge focusing on collecting clinical data closely linked to gene sequencing aimed at improving clinical trial design. Through our consortium initiatives, new therapeutic targets will be identified leading to new treatment approaches.

Treatments that significantly change the course of ALS and ultimately halt the disease continue to be a high priority in our programs. Improving the lives of people living with ALS is also a primary focus. In recognition of the interdependence of care and research, we will continue to leverage our clinical network to conduct a variety qualitative and quantitative research with our clinics to help to improve patient care, communications, and mobility for those living with ALS.



# IMPACT ON RESEARCH

## The ALS Ice Bucket Challenge

### THE ALS ICE BUCKET CHALLENGE

In August 2014, millions of people around the world dumped buckets of ice water on their heads to raise awareness and funds in support of the ALS community. The result was staggering – The ALS Association welcomed 2.5 million new donors, the majority of them millennials, and received \$115 million in just six weeks; at least \$100 million more was donated to other ALS organizations around the world. It was the most important moment in the history of ALS since Lou Gehrig's farewell speech more than 75 years ago. Ultimately, the ALS Ice Bucket Challenge became the single biggest act of collaborative grassroots fundraising in history. This all stemmed from the efforts of three young men living with ALS, who inspired their communities, celebrities, and the world to join the fight against, and bring awareness to this devastating disease.



***The ALS Ice Bucket Challenge became the single biggest act of collaborative grassroots fundraising in history.***

### ALS ICE BUCKET CHALLENGE AND RESEARCH

The ALS Ice Bucket Challenge and the infusion of funding it generated has had a significant impact on advancing ALS research globally. Since 2014, The ALS Association has invested more than \$89 million in the most promising research projects. The ALS Association research budget more than tripled to an all-time high of \$19 million, which propelled the organization to become the largest ALS research funder outside the U.S. federal government in any single year in the world. We proudly fund diverse, cutting-edge research through our competitive TREAT ALSTM™ global research program in laboratories around the world, rather than just one laboratory. With your help, we funded more than 180 critical projects in 11 countries in the last year alone, in addition to a total of nine global collaborative initiatives that would not have been possible without the ALS Ice Bucket Challenge. Through collaborations with government, industry, academia, and other nonprofit organizations, The ALS Association aims to accelerate drug development so that people living with ALS receive treatments faster.

# RESEARCH

## Our Strategic Initiatives

The ALS Association has announced nine important research strategic initiatives since the ALS Ice Bucket Challenge to advance the search for treatments and a cure for the disease. In this document, we have included details on the goals of each initiative, along with information on The ALS Association's role and funding commitments.

Strategic initiatives are large global collaborations focused on the understanding of the disease, targeting new therapies, expediting clinical trials, and making RNA and DNA sequencing data available to the entire ALS research community. These initiatives will generate data and resources available for researchers globally. Central to all the major new collaborations are the people living with ALS.

Learn more about each strategic initiative here:

<http://www.alsa.org/research/our-approach/inspiring-partnerships/strategic-initiatives/>

### PROJECT MINE

#### **\$1.4 million commitment partnered with Greater New York and Georgia Chapters**

An international, large-scale research initiative devoted to discovering genetic causes of ALS and to ultimately finding a cure. The goal is to identify [genes](#) associated with ALS by performing whole genome sequencing on at least 15,000 ALS patients plus 7,500 healthy controls worldwide, resulting in an open-source ALS genome database, in conjunction with the collection of skin samples to make ALS patient-induced pluripotent stem cell (iPSC) lines. Our funding supports the U.S. arm of this initiative, led by Jonathan Glass, M.D. (Emory University) and John Landers, Ph.D. (University of Massachusetts Medical School). [Funding announced in October 2014.](#)

### NEWYORKGENOMECENTER – CENTER FOR GENOMICS OF NEURODEGENERATIVE DISEASES (NYGC CGND)

#### **\$2.5 million commitment partnered with Greater New York Chapter matched with an additional \$2.5 million contributed by the Tow Foundation**

A [consortium](#) that is a collaboration between numerous global laboratories capable of generating and analyzing thousands of DNA sequences from people with ALS. The goal is to discover new genetic contributors of ALS to then translate into clinical solutions for ALS. It houses all data in a central repository that is freely available to the research community worldwide. [Funding announced in October 2014.](#)

### GENOMIC TRANSLATION FOR ALS CARE (GTAC)

#### **\$3.5 million commitment partnered with Greater New York Chapter**

A collaboration between Biogen and Columbia University Medical Center (CUMC) to better identify new targets for treatment development, in order to understand how different genes contribute to various clinical forms of ALS. This will translate into clinical trials that are more focused. This [project](#) will follow 1,500 people with ALS

and collect detailed clinical data, sequence their DNA and store blood cell samples to generate iPSCs. This study will allow correlation of ALS clinical symptoms to genetic causes and help stratify patients for future clinical trials. [Funding announced in August 2015.](#)

## CReATe

**Clinical Research in ALS and Related Disorders for Therapeutic Development (CReATe) Consortium: \$450K commitment for biomarker study and biorepository and an \$835,937 commitment to Drs. Paul Taylor, Jinghui Zhang, and Michael Benatar for DNA sequencing**

A Rare Diseases Clinical Research Consortium (RDCRC) that forms part of the National Institutes of Health (NIH) Rare Diseases Clinical Research Network. The goal of CReATe is to identify new genes and novel disease pathways linked to ALS and related disorders. In addition to sequencing samples collected from study participants, CReATe is building a resource of biosamples that have attached detailed clinical information, providing a unique and critical resource for biomarker development. The biorepository will enable the discovery and validation of biomarkers relevant to therapy development for patients with ALS and related disorders. In partnership with The ALS Association, CReATe is funding pilot biomarker projects using this resource, as well as other biorepositories, including the Northeast ALS Consortium (NEALS) biorepository supported by The ALS Association. [Funding announced September 2015.](#)



- **CReATe Connect: All ALS organizations associated with CReATe are a part of Connect**

A part of the Rare Diseases Clinical Research Network (RDCRN) Contact Registry, CReATe Connect is an international online system to help facilitate communication between doctors/scientists and patients and their families. CReATe Connect provides a means for patients with these rare diseases (and their family members) to indicate their willingness to be contacted in the future about clinical research opportunities and to receive updates on the progress of research and new educational opportunities sponsored by [CReATe](#).

## NEUROLINCS

**\$2.5 million commitment partnered with the Greater Philadelphia Chapter**

A partnership with NIH's National Institutes of Neurological Disorders and Stroke (NINDS). This National Institutes of Health (NIH)-funded collaborative effort is between various research groups with expertise in iPSC technology, disease modeling, OMICS methods, and computational biology. The goal is to use iPSC lines from ALS patients and healthy controls and OMICS methods to identify unique cell signatures that are specific to various subtypes of motor neuron diseases, in order to better develop therapies and design clinical trials. [Funding announced July 2016.](#)

## ALS ACCELERATED THERAPEUTICS (ALS ACT)

**\$10 million commitment matched with an additional \$10 million contributed by ALS Finding a Cure®**

A novel academic-foundation-industry partnership with ALS Finding a Cure, initiated with researchers from

General Electric (GE) Healthcare and four academic NEALS sites to accelerate treatments for people living with ALS. It is using the following strategies to develop new therapeutic approaches for ALS: supporting development of neuroimaging tools as potential ALS biomarkers; supporting projects focused on decreasing the production of misfolded proteins, and reversing neuroinflammation, two major contributors to the disease process; supports NeuroBANK™ (see below); and supporting Phase IIA pilot clinical trials with relevant biomarkers aimed at developing novel high-potential ALS treatments. A [TDP 43 PET Tracer Grand Challenge](#) was launched as part of ALS ACT. [Funding announced October 2014.](#)



- **NeuroBANK™: funding under ALS ACT – [further expanded in August 2016](#)**

A patient-centric clinical research platform and central repository that sets the framework to allow for standardization of ALS patient information (including proteomic, genomic, and clinical data) that is linked across simultaneously running research studies, locations, and modalities. It is designed to host, curate, and disseminate this information. Global Unique Identifier (GUID) technology generates a patient-specific character string that securely identifies a patient without revealing their true identity. Neurobank™ is part of NYGC projects, GTAC, and Answer ALS.

## NEURO COLLABORATIVE

**A \$5 million commitment in October 2014 - funding through The ALS Association with contributions from the Orange County and Wisconsin Chapters. To date, we have committed a total of \$8 million.**

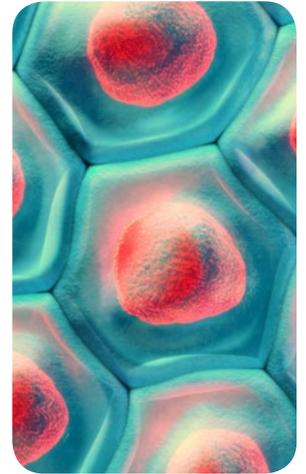
An initiative founded as a collaboration between three leading California laboratories aimed at discovering and developing new potential ALS therapies that can be delivered to pharmaceutical companies for further development. The three laboratories are the Svendsen Laboratory at Cedars-Sinai in Los Angeles, which will develop and maintain a Motor Neuron Core Facility to create iPSC lines from people with ALS that will be openly shared; the Cleveland Laboratory at the University of California San Diego, which will spearhead the development of antisense therapy against the C9orf72 gene, the most common genetic cause of ALS; and the Finkbeiner laboratory at the Gladstone Institutes, which is affiliated with University of California San Francisco, which will further develop robotic technology for screening drugs in motor neuron cell culture. The Cleveland laboratory is collaborating with Martin Marsala, M.D., at the University of California San Diego and Brian Kaspar, Ph.D., at the Research Institute at Nationwide Children's Hospital in Ohio. In 2014, The ALS Association Golden West Chapter, along with Advisory Trustees Jim Barber and Linda Della, partnered with the National ALS Association to build the Neuro Collaborative concept. For more information, [click here](#).

[Funding announced October 2014.](#)

## ANSWER ALS

**The ALS Association contributed to its development/business plan and is a partner with Team Gleason and others to advance this initiative. We plan to contribute funds as the program evolves.**

An initiative spearheaded by Steve Gleason to challenge ALS researchers to come up with a solid plan to find a cure for ALS. Its strategy includes two impact goal arms. One is designed for immediate impact to help ALS patients live more productive lives by supporting affordable assistive technologies and services. The other arm is designed to contribute to the ultimate impact to fund a collaborative effort to bring together the world's best ALS researchers to find a treatment or a cure in the next five-10 years. As part of this initiative, all DNA samples from participants will be sequenced by the New York Genome Center (NYGC), which will be funded through ALS Association research programs. In addition, NeuroBANK™ will be an integral part of the program. Projects funded as part of ALS ACT, the Neuro Collaborative, and NeuroLINCS form an important foundation for Answer ALS. [Partnership announced in September 2015.](#)



## ALS ONE – MASSACHUSETTS ALS PARTNERSHIP

**The ALS Association partnered with ALS ONE and ALS Finding a Cure to fund \$2 million each for specific clinical and research initiatives to maximize collaborations to find treatments and a cure for ALS.**

An initiative founded by Kevin Gosnell, a person who passed away from ALS, to bring together leading neurology experts and care specialists in Massachusetts to leverage their institutions' strengths to expedite progress toward finding a treatment for ALS by 2020 while improving care now. Institutional partnerships include Massachusetts General Hospital, the ALS Therapy Development Institute (ALS TDI), the University of Massachusetts Medical School, and Compassionate Care ALS. Under the ALS ONE umbrella, we fund research projects of Dr. Steven Perrin from ALS TDI, Dr. Nazem Atassi from Mass General, and Dr. Robert Brown from U. Mass Medical School. [Partnership announced January 2016.](#) [Funding announced in November 2016.](#)

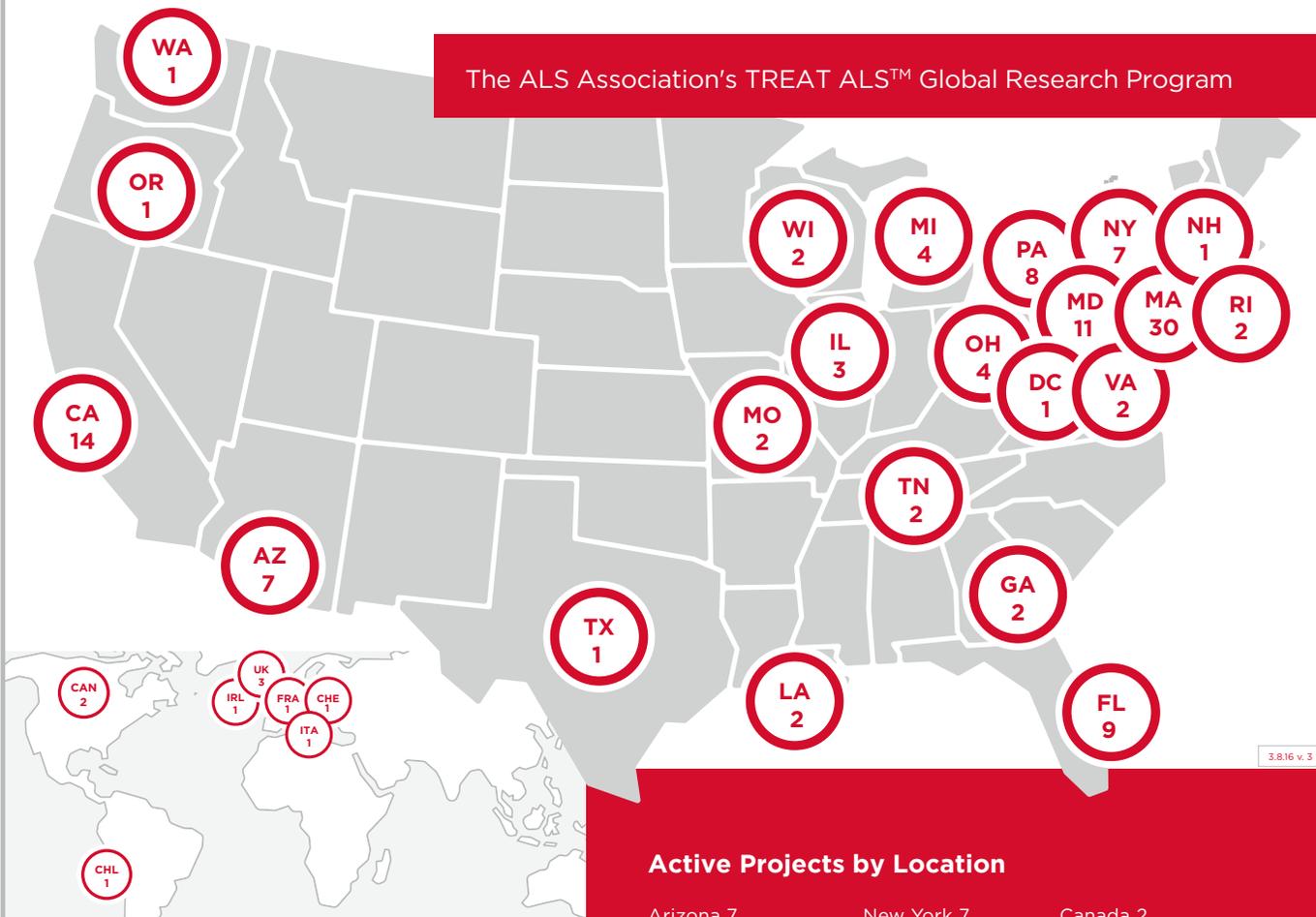


## SECTION 2: INFOGRAPHICS

# CURRENT PROJECTS

The ALS Association Is Accelerating Progress Toward Treatments

The ALS Association's TREAT ALS™ Global Research Program



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**126** Active Research Projects

In an effort to accelerate progress toward finding treatments and a cure for ALS, The ALS Association is currently funding 126 active research projects all over the globe.

## Active Projects by Location

- |                  |                |                  |
|------------------|----------------|------------------|
| Arizona 7        | New York 7     | Canada 2         |
| California 14    | Ohio 4         | Chile 1          |
| D.C. 1           | Oregon 1       | France 1         |
| Florida 9        | Pennsylvania 8 | Ireland 1        |
| Georgia 2        | Rhode Island 2 | Italy 1          |
| Illinois 3       | Tennessee 2    | Switzerland 1    |
| Louisiana 2      | Texas 1        | United Kingdom 3 |
| Massachusetts 30 | Virginia 2     |                  |
| Maryland 11      | Washington 1   |                  |
| Michigan 4       | Wisconsin 2    |                  |
| Missouri 2       |                |                  |
| New Hampshire 1  |                |                  |

**ALS**  
ASSOCIATION

# ACCELERATING THE SEARCH FOR A CURE

The ALS Association Is Funding Scientific Projects across the Research Pipeline

We support a wide breadth of scientific focus areas – each is critical to advancing ALS research.



## Harnessing Innovative Ideas:

Basic research at the lab bench to find therapeutic targets



## Translating Concepts to Therapies:

Drug development and biomarker discovery



## Advancing Treatments to Patients:

Clinical trials, assistive technology, patient care

## Thirteen Scientific Focus Areas

- Disease Mechanisms
- Environmental Factors / Epidemiology
- Disease Models
- Genetics
- Cognitive Studies
- Natural History Studies
- Assistive Technology
- Clinical Studies
- Stem Cells
- Precision Medicine
- Biomarkers
- Drug Development
- Nanotechnology

For more information, visit:

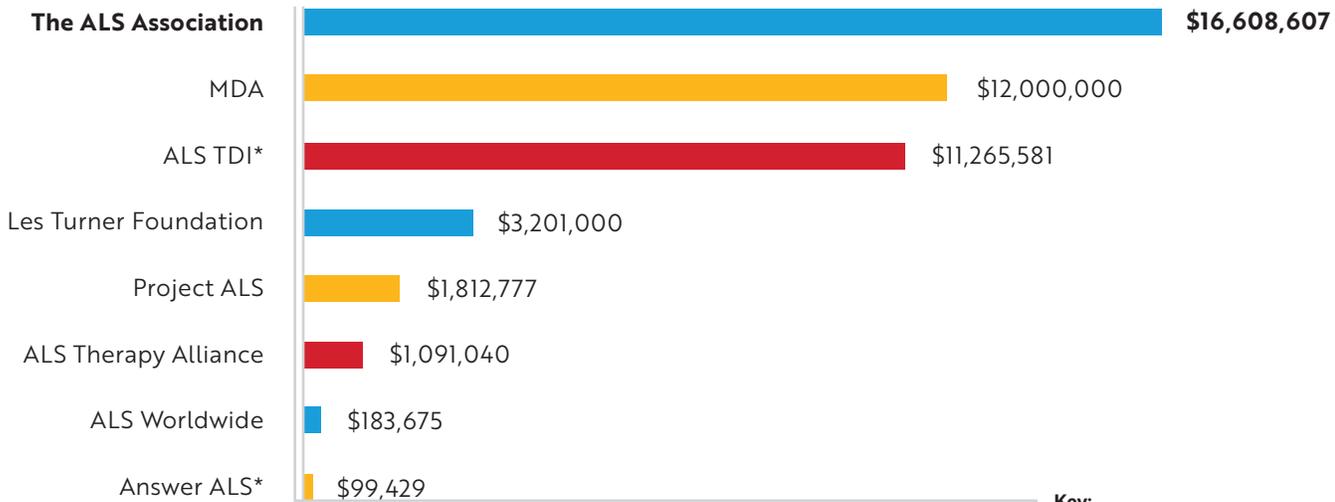
[www.alsa.org/research/our-approach](http://www.alsa.org/research/our-approach)

[www.alsa.org/research/focus-areas](http://www.alsa.org/research/focus-areas)

# 2015 NONPROFIT SPENDING ON RESEARCH

The ALS Association Is the Largest Nonprofit Funder of ALS Research in the U.S.

## 2015 Nonprofit Spending on ALS Research



Research Dollars Spent on ALS Scientific Discovery

Information from 990/annual report finances from 2015

Note: Graph represents funding supporting approved peer-reviewed research grants

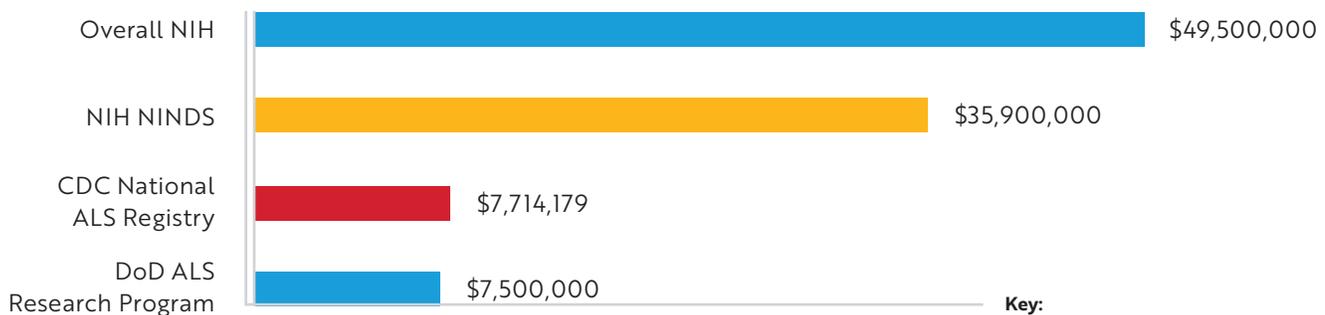
\*ALS TDI & Answer ALS = total program service expenses to operate. They do not fund outside research grants

**Key:**

MDA: Muscular Dystrophy Association  
ALS TDI: ALS Therapy Development Institute

# 2015 FEDERAL GOVERNMENT SPENDING ON RESEARCH

The ALS Association Leads the Effort in Advocating U.S. Government Spending in ALS Research.



Research Dollars Spent on ALS Scientific Discovery

Note: In 2015, the NIH invested \$49.5 million in ALS research, of which \$35.9 million was from the NINDS. Also, in 2015, the CDC was appropriated \$7.7 million for the National ALS Registry and the DoD was appropriated \$7.5 million for the ALS Research Program

**Key:**

NIH: National Institutes of Health  
NINDS: National Institute of Neurological Disorders and Stroke  
CDC: Centers for Disease Control and Prevention  
DoD: Department of Defense

# ALS RESEARCH

## 2017 Priorities and Current Statistics

The ALS Association's collaborative and global approach to funding research continues to lead to significant advances by top ALS researchers all over the world.

### THE WORLD IS OUR LAB

We fund novel, promising research around the globe covering all scientific focus areas, spurring innovation along the way.



 **126+** FUNDED GLOBAL RESEARCH PROJECTS IN 8 COUNTRIES

**\$18 MILLION**  current research budget  
*The ALS Association is the highest nonprofit research funder in the U.S.*

**9** global strategic initiatives 

**2** Clinician Scientists Funded in 2017 

**6** new Postdoctoral Fellows Funded in 2017 

 **4 NEW GENES** identified since the ALS Ice Bucket Challenge (IBC) to develop new therapies

**55+** actively recruiting ALS clinical trials 

**\$89+ MILLION**  dedicated to research since the ALS IBC to advance treatments and a cure

 two potential new antisense drugs and numerous other drugs on the horizon aimed to slow or stop the progression of ALS



# RESEARCH STRATEGY

## A Collaborative and Global Approach That Equals Immense Impact

Our program is far-reaching, innovative, collaborative, and powerful.



### INSPIRING PARTNERSHIPS

Collaboration is the cornerstone of our research program. We partner with academia, industry, government, and other nonprofit organizations.

**Impact:** We lead by spurring long-lasting collaborations among researchers across all sectors, leading to globally shared data, protocols, and research samples to accelerate research progress.



### ATTRACTING YOUNG, BRIGHT SCIENTISTS

We encourage young scientists to enter and remain in ALS research and are dedicated to their continued success.

**Impact:** Over 90 percent of our postdocs remain in ALS research to start their own labs and mentor more young researchers.



### INVESTING IN CLINICAL TRIALS

We sponsor ALS clinical trials to accelerate drugs through the drug pipeline as quickly as possible.

**Impact:** Currently, we are funding eight ALS interventional clinical trials. We have helped countless drugs move from ideas into trials. Cedars-Sinai's combined stem cell-gene therapy trial, which started this year, is just one example.



### MAXIMIZING INVESTMENTS

We secure matching gifts to significantly increase donor investment from the ALS IBC and beyond.

**Impact:** Our original \$1.5 million investment in antisense technology infused an additional \$100 million and one FDA-approved drug for spinal muscular atrophy, SPINRAZA™, and two potential new ALS drugs targeting SOD1 and C9orf72.



### WORKING WITH TOP ALS EXPERTS

We collaborate with top ALS scientists, clinicians, consultants, entrepreneurs, and executives to create and lead an exceptional research program.

**Impact:** Our highly competitive research program funds the most ALS research dollars of any ALS nonprofit, \$19 million in 2016, and is held to rigorous standards to drive innovation.



### CHAMPIONING PEOPLE LIVING WITH ALS

People living with ALS are at the center of everything we do and must receive the best care and support possible.

**Impact:** Last year, we funded five clinical management projects focused on improving care for people living with ALS and their families. We awarded two winners of the ALS Assistive Technology Challenge, driving innovation!

# GRANT PORTFOLIO

## The ALS Association Provides Funding at Every Stage of the Research Pipeline

Thanks to our generous donors, The ALS Association awards various research projects throughout the year as part of its competitive Translational Research for ALS (TREAT ALS™) Portfolio, which include the following:

- **Multiyear Investigator-Initiated Grants** to established investigators.
- **One-year Starter Grants** to investigators new to the ALS field or senior postdoctoral fellows establishing their own independent position.
- **Milton Safenowitz Postdoctoral Fellowships** to encourage and facilitate promising young scientists to enter the ALS field. Fellows work with a senior mentor and receive extensive exposure to the ALS research community through meetings and presentations.
- **Strategic Challenges** are crowdsourcing initiatives such as the ALS Assistive Technology Challenge to help people living with ALS communicate with ease (partnered with Prize4Life) and the TDP43 PET Tracer Grand Challenge to discover a biomarker to track TDP43 in the body (partnered with ALS Finding a Cure®).
- **Strategic Calls** that invite researchers to submit collaborative projects that address research gaps, areas of high risk-high reward, and/or areas that provide novel opportunities. Includes funding of **Strategic Initiatives** that are large, collaborative research programs. For more information, visit the strategic initiative page and refer to the strategic initiative talking points.
- **Clinical Development Fellowships**, in partnership with the American Academy of Neurology (AAN), to support ALS clinician-researchers focused on projects involving people living with ALS.



- **Lawrence and Isabel Barnett Drug Development Program** fosters collaborations with companies/academia to fund milestone-driven research focused on preclinical studies to move treatment approaches closer to the clinic. Funding specifications and project criteria vary for each specific request for proposals.
- **Pilot Clinical Trials** to support up to and including phase II clinical trials that are associated with a comprehensive biomarker program to test novel, high-potential treatment approaches in people with ALS.
- **Clinical Management Awards** to fund research for improving clinical, psychological, and social management of ALS, focusing on both people living with ALS and their caregivers.

For questions, please contact Dr. Lucie Bruijn, ALS Association Chief Scientist, at [lucie@alsa-national.org](mailto:lucie@alsa-national.org).



**SECTION 3:  
DEVELOPMENT**

# BIOMARKER FUNDING OPPORTUNITIES

## Developing a Faster, More Accurate Diagnosis

Biomarkers are any measurable substance that changes in quantity, either appearing or disappearing over time, with a change in the body's state. Examples are a chemical change in your blood, urine or cerebral spinal fluid, and structural change or chemical change in your brain. They are used to diagnose diseases and track effectiveness of potential treatments. Currently, there are no approved biomarkers for ALS. **The ALS Association currently funds 34 active biomarker projects with a total contribution of approximately \$17 million in grants.**

### IMPACT ON ALS

Today, researchers rely on clinical trial outcome measures such as the ALS Functional Rating Scale – Revised (ALSF<sub>RS</sub>-R), forced vital capacity (FVC), and others. Once developed, their potential is immense. Right now, the average time to ALS diagnosis is one year. We need to do better. Biomarkers will make ALS diagnosis faster and more accurate. They will also allow physicians the ability to track the disease in real time as ALS progresses in a patient, allowing for more proactive and targeted care. Clinical trials will be more easily stratified, allowing clinicians to test specific populations of people that have a high potential for the therapy to be effective. Biomarkers will also be used to track a person's response to therapy. It will show whether a drug is hitting its target in the central nervous system and is working properly. Biomarkers will accelerate drug development of new treatment for ALS by making the clinical trials more efficient. This, in turn, increases a potential therapy's value to pharmaceutical companies, as it will be readily apparent if the therapy is working as designed.



*“The ALS Association is committed to supporting biomarker discovery. Identifying biomarkers is an extremely important step in the drug development pipeline to accelerate the discovery of novel treatments and a cure for ALS. We support a number of exciting biomarker research studies in addition to the TDP-43 Biomarker Grand Challenge, all aimed at pioneering and moving the ALS biomarker field rapidly forward.”*

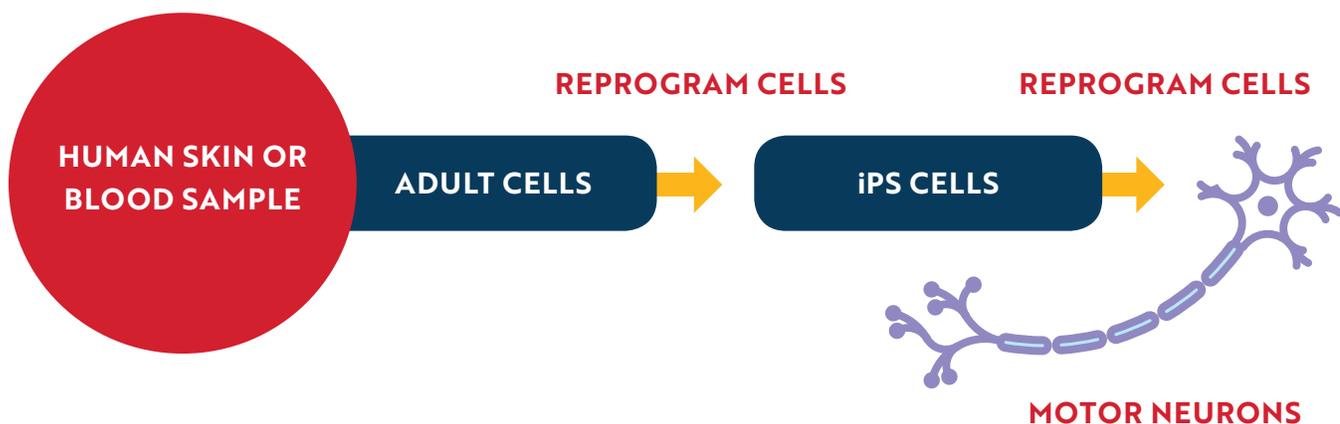
*– Chief Scientist Dr. Lucie Bruijn*

# STEM CELLS

## Exceptional Tools to Find New Treatments

Stem cells have the ability to divide for indefinite periods in a dish, providing an unlimited supply of cells to study. They can give rise to any specialized cell type in the body, including motor neurons and support neurons called glia, which are both lost in ALS. There are different types of stem cells, such as induced pluripotent stem cells (iPSCs), which are typically created from adult skin cells or blood. When derived from a person living with ALS, iPSCs are transformed into motor neurons, exactly reflecting the person's genetic makeup – like an avatar in a dish.

**The ALS Association currently funds 16 stem cell grants with a total contribution of approximately \$11 million.**



### IMPACT ON ALS

iPSCs have emerged as the most significant source of stem cells for ALS research and are important sources of neurons to model the disease in a dish. They have the potential to identify new disease pathways and individual susceptibilities to disease that cannot be revealed with other models. They serve as exceptionally valuable tools to find new treatments based on a person's unique genetic makeup. Neurons derived from iPSCs can be tagged with fluorescent markers to allow tracking of individual neurons over time. This allows researchers to conduct drug screens to find compounds that improve the health of neurons, identifying a potential therapy. Motor neurons derived from iPSCs are even being used in parallel to people living with ALS (from which the cells are derived) during clinical trials to help predict whether a trial drug will positively impact the health of motor neurons.

***"iPSCs have emerged as exceptionally valuable tools for modeling disease, screening for new therapies, and finding new treatments based on a person's unique genetic makeup."***

– Dr. Lucie Bruijn, Chief Scientist, The ALS Association

# GENETICS

## Working to Close the Genetic Gap

Researchers have demonstrated that 10 percent of ALS cases are familial, meaning the disease gene is inherited. The other 90 percent of ALS cases are sporadic, meaning they do not know the underlying cause. It is likely that a percentage of the sporadic cases are familial, but those genes are yet to be uncovered. In recent years, there has been a large boom in genome sequencing (where all of a person's DNA is sequenced) due to decreased cost (approximately \$2,000 per genome) and advances in sequencing technology. Currently, more than 30 ALS genes have been identified, and counting. The ALS Association supports big initiatives all over the world that are working toward closing the genetic gap to identify all possible ALS genes.

**The ALS Association currently funds 12 genetics grants with a total contribution of approximately \$10 million.**



### IMPACT ON ALS

Gene discovery represents opportunities for new therapeutic targets, thereby increasing the number of potential ALS therapies. Importantly, insights gained from studying genetic forms of ALS are likely to benefit those with sporadic ALS. For example, new model organisms based on newly identified genes are developed to better understand and discover novel disease pathways – information that can be tested and possibly applied to all ALS cases. These new genetic discoveries allow scientists to study disease in ways that would otherwise not have been possible. In addition, identified genetic mutations can be corrected using cutting-edge gene therapy that aims to slow or stop the progression of ALS. Antisense technology designed to correct the two most commonly inherited genes – SOD1 and C9orf72 – is in clinical and preclinical trial phases, respectively. New gene editing technology, such as CRISPR, may also add value in the ALS treatment landscape.

***“The ALS Association is committed to supporting genome sequencing and the next frontier of gene discovery. The more genes we uncover, the more potential therapeutic targets we will have, leading us closer to our goal – to discover effective treatments and a cure for this devastating disease.”***

– Dr. Lucie Bruijn, Chief Scientist of The ALS Association

# INNOVATIONS IN ALS

## 2016's Top 10 Biggest Advances

In 2016, a significant number of ALS research discoveries, advances in clinical trials, collaborations, and strategic initiatives all accelerated the pace of discovery in finding treatments and a cure for ALS.

**Here are 10 of 2016's BIGGEST advances in ALS research! Seven out of 10 were funded by The ALS Association.**

### Radicava™

1. The U.S. Food and Drug Administration (FDA) [reviews and accepts a New Drug Application \(NDA\)](#) for Radicava™ for the treatment of ALS in 2016. On May 5, 2017, the FDA [approves](#) Radicava™ – the first treatment for ALS in over 20 years. With our ALS Drug Development Guidance document in hand, the ALS Association's Advocacy team worked with the FDA to speed the approval process. It is yet to be seen how Radicava™ will impact people with ALS in the U.S.

### PET Imaging\*

2. The Neurological Clinical Research Institute (NCRI) imaging team at Massachusetts General Hospital (MGH) led by Dr. Nazem Atassi, supported under The ALS Association's ALS ACT, uses **PET (Positron Emission Tomography) imaging to successfully scan the first person living with ALS to measure inflammation in the brain**, a promising first step in this imaging biomarker study. Since then, many more people have participated in the study.

### Spt4\*

3. [Dr. Aaron Gitler](#) and his researcher colleagues, supported by The ALS Association, **identifies a new therapeutic target called Spt4**, designed to reduce toxicity associated with C9orf72 ALS, adding to the growing list of potential ALS therapeutics.

### STEM CELL-GENE THERAPY\*

4. Investigators at Cedars-Sinai [gain approval from the FDA](#) to test the safety of a **combination stem cell–gene therapy in a clinical trial** that began in 2017—research the The ALS Association has supported since 2003. Cedars-Sinai is a certified Treatment Center of Excellence, meeting The ALS Association's rigorous standards with their comprehensive, collaborative approach to patient care and services.

### NEK1\*

5. The **discovery of the NEK1 gene**, now known to be among the most common genes that contribute to the development of ALS, [makes headlines around the globe](#). More than 80 researchers in 11 countries out of Association-supported Project MinE conducted the largest-ever study of inherited ALS. This discovery of NEK1 has provided researchers with an important new target for therapy development.

### Big Data

6. IBM's Watson [supercomputer discovers five new ALS genes](#). IBM's collaboration with the Barrow Neurological Institute in Phoenix shows **the power of Big Data** and the potential for advanced computing to speed up progress toward treatments and a cure.

### ALS ONE & NeuroLINCS\*

7. **Global collaborations ALS ONE and NeuroLINCS are announced**, [supported by millions in funding from The ALS Association](#). These two initiatives will leverage resources and help generate the data researchers need to continue their important work.

### NurOwn®

8. Brainstorm Cell Therapeutics reports **positive results in the NurOwn® stem cell phase II trial in the U.S.** and then [announces a larger phase III trial to begin in 2017](#).

### GTAC\*

9. One of the nation's **largest precision medicine programs, Genomic Translation for ALS Care (GTAC)**, begins enrollment in October 2016, in collaboration with nine centers at universities and hospitals across the United States. [The ALS Association committed \\$3.5 million in Ice Bucket Challenge-raised money to this exciting collaborative effort](#).

### Phase II trial of Arimoclomol\*

10. At the International ALS/MND Symposium in Dublin, a leading University of Miami ALS researcher and the pharmaceutical company [Orphazyme announce](#) the successful completion of a **phase II trial of Arimoclomol** for inherited SOD1-ALS. The ALS Association has long supported this trial to move the needle forward for people living with familial ALS.

# SCIENTIFIC FOCUS AREAS

## The ALS Association Commitment

The ALS Association supports a wide breadth of specific fields of study that are critical to advancing ALS research. We are always on the lookout for the next cutting-edge field to invest in.



### BIOMARKERS

The ALS Association is committed to biomarker discovery, as their potential is immense. Identifying biomarkers is vital to improving diagnosis, following disease progression, tracking response to therapy, and make clinical trials more efficient. Our support of the TDP-43 Biomarker Grand Challenge Program is just one example.



### NATURAL HISTORY STUDIES

These studies are important to understanding the natural disease course of familial (inherited) ALS. The ALS Association is supporting several natural history studies of SOD1 and C9orf72 ALS, which are critical to helping inform patient care and clinical testing of new treatment approaches.



### ASSISTIVE TECHNOLOGY

The ALS Association is working to develop accessible, portable devices for people living with ALS, in order to help them maintain a high quality of life. The ALS Assistive Technology Challenge winners we announced in December 2016 are dedicated to achieving this!



### CLINICAL STUDIES

The ALS Association supports clinical management grants to improve the lives of people living with ALS and their caregivers, along with clinical trials to accelerate treatments through the drug development pipeline.



### ENVIRONMENTAL FACTORS

Multiple factors in one's lifestyle and surroundings, such as smoking and military service, are the only known ALS risk factors. The ALS Association champions multiple efforts to better understand these risk factors and drive discovery of other factors that may contribute to ALS.



### COGNITIVE STUDIES

There is a great deal of evidence that cognitive impairment is connected to ALS, such as overlap with frontotemporal dementia (FTD). The ALS Association is committed to improving understanding of why and how this connection takes place.



## GENETICS

The number of genes identified to cause familial ALS has multiplied since the discovery of SOD1. Many efforts are underway to identify more ALS genes and target them for therapy. The ALS Association continues to make significant investments in identifying new genes and has supported all the major ALS gene discoveries in history.



## DISEASE MECHANISMS

ALS is a complicated disease involving multiple disease pathways. The ALS Association encourages research to discover novel pathways. Understanding how ALS disease works on many biological levels is necessary to identify potential therapeutic targets.



## NANOTECHNOLOGY

There is growing interest in using nanotechnology as a delivery tool for ALS therapeutics, and we are on the cutting edge, funding this exciting technology.



## DRUG DEVELOPMENT

The ALS Association is supporting development of several different treatment approaches, including small molecules, stem cells, and gene therapy. Our early support of antisense drugs in 2004 has paid off! Antisense therapies have already proven effective in spinal muscular atrophy (SMA), are in trial for SOD1 and are starting in the near future targeting C9orf72.



## STEM CELLS

Stem cell technology is progressing rapidly, and The ALS Association is spearheading work on several critical fronts to advance this key research tool.



## DISEASE MODELS

The ALS Association's research portfolio supports a variety of model systems used for understanding disease pathways and testing promising compounds.



## PRECISION MEDICINE

The ALS Association has helped establish and currently supports several partnerships and precision medicine programs to aid in the identification of new disease genes and targets for drug therapy.

Learn more on the [Scientific Focus Area Page](#).