Dear Friends:

After losing my father to Alzheimer’s disease, a friend of mine said to me: “There are so many of us who have been touched by Alzheimer’s. You need to do a fundraising event.” So, I pulled together a committee of people who I knew were affected by Alzheimer’s to plan a fundraiser for the Alzheimer’s Association. Initially, I wasn’t sure if the event would be successful, but it sold out immediately and we raised $2 million out of the gate. This made me realize that there was a willingness to help fight this disease that none of us had imagined. That’s when Part the Cloud was born.

Fast forward 12 years: That inaugural local Bay Area event has morphed into a global movement that has generated more than $68 million dollars and funded 65 groundbreaking and innovative clinical trials across the globe in nine countries. Part the Cloud provides key funding for early-phase clinical trials and serves as a catalyst for researchers to obtain additional funding for their work. After initial funding from Part the Cloud, grant recipients have gone on to receive more than $1.3 billion in follow-on funding from the federal government, venture capital firms and other sources.

In a continued effort to be at the forefront of science, Part the Cloud has launched a new fundraising initiative — the Gene Targeting Challenge — to supercharge the development of therapies tailored to the genetic underpinnings of Alzheimer’s disease. This challenge, which will support new and ongoing early-stage clinical trials using gene targeting, is what Part the Cloud does best: investing in big, bold ideas that will move the needle in our quest to end Alzheimer’s and all other dementia. In this impact report, you’ll read more about the new Gene Targeting Challenge, as well as Part the Cloud’s current global impact on the Alzheimer’s drug pipeline broadly.

I founded Part the Cloud with a singular mission: to end Alzheimer’s disease. While we’ve already accomplished so much, there’s a long road ahead of us. But with the continued innovation of this program and support from our generous donors, I’m confident we will reach the finish line.

Thank you for your steadfast support. Together we will Part the Cloud!

Warmly,

Mikey Hoag
Dear Friends,

The year 2023 proved to be yet another historic year in the fight against Alzheimer’s disease and all dementia. We had the first traditionally approved treatment that targets the underlying biology for people in early stages of Alzheimer’s, as well as a commitment from the Centers for Medicare and Medicaid services (CMS) that traditionally approved treatments will receive coverage. With this progress, and the strides made through visionary initiatives such as Part the Cloud, we’re no longer approaching the new era of treatment – we’re in the new era of treatment.

But there’s more work to do — critical work. More than 6 million Americans are living with Alzheimer’s. By 2050, this number is projected to rise to nearly 13 million. It is the sixth-leading cause of death in the US. In the last 20 years, deaths from heart disease have decreased 7.3% while deaths from Alzheimer’s have increased 145%.

With soaring prevalence and enormous costs, Alzheimer’s is an escalating global health crisis, and now is the time. Treatments that target Alzheimer’s from all angles and all stages of the disease are essential, and that’s why strategic research funding that works to diversify the drug pipeline is so important.

The Alzheimer’s Association is so proud of the role Part the Cloud has taken to expand the pipeline and support the global research community. By funding high-risk, high-reward research projects, Part the Cloud fills a hole in Alzheimer’s research. We must leave no stone unturned when it comes to finding treatments for Alzheimer’s and all other dementia, and Part the Cloud is designed to explore every feasible option in order to drive research forward to get potential treatment options to people living with Alzheimer’s faster.

This work would not happen without the commitment of philanthropic leaders such as Mikey Hoag and the generous support of our donors. Through them — and all of you — we are able to support these early-phase clinical trials by accelerating the translation of findings from the laboratory, through trials, into possible therapies.

There is light at the end of the tunnel — and that’s because of you. The Alzheimer’s Association is grateful for your generosity and support.

Sincerely,

Joanne Pike, DrPH
TRANSLATIONAL RESEARCH GRANT RECIPIENTS

Part the Cloud awards grants to scientists focusing on a wide range of research areas.

Metabolic Function
how neurons process energy

Amyloid Plaques and Tau Tangles
hallmarks of Alzheimer’s disease

The Immune Response, Misfolded Proteins and Growth Factors in the Brain
how the brain heals

Cell Signaling and Communication
how brain cells talk to one another

Vascular
blood vessels and blood flow to the brain

Oxidative Stress
imbalance between oxidants and antioxidants

Cell Senescence
how cells age, and how to address the effects of cellular aging

Genome Sequencing
gene mapping

GENOME SEQUENCING

Michael Weiner, M.D.
University of California at San Francisco - San Francisco, CA

*Part the Cloud supported, in part, the Whole Genome Sequencing Alzheimer’s Disease Neuroimaging Initiative (WGS-ADNI), a project to sequence the whole genome of more than 800 individuals.*
CELL SENESCENCE

James Kirkland, M.D., Ph.D.
Mayo Clinic - Rochester, MN
ALSENLITE: An Open-Label Pilot Study of Senolytics for Alzheimer’s Disease

Maurice Zauderer, Ph.D.
Vaccinex, Inc. - Rochester, NY
SEMA4D Blockade Safety and Brain Metabolic Activity in Alzheimer’s Disease

IMMUNE RESPONSE, MISFOLDED PROTEINS AND GROWTH FACTORS

Steven Arnold, M.D.
Massachusetts General Hospital - Boston, MA
BCG Immunization Effects on Biomarkers of Inflammation/Immune Response and Alzheimer’s Disease

Hung-Kai (Kevin) Chen, M.D., Ph.D.
Elixiron Immunotherapeutics Inc. - Taipei, Taiwan
Modulating Neuroinflammation by Targeting Microglia with CSF1R Inhibitor EI1071
*Two-time grant winner*

John Sedivy, Ph.D.
Brown University - Providence, RI
Repurposing Nucleoside Reverse Transcriptase Inhibitors for Treatment of Alzheimer’s Disease

Joseph Foss, M.D.
NeuroTherapia, Inc. - Cleveland, OH
A Phase I Single Ascending Dose Safety and Pharmacokinetic Study of NTRX-07

Franz Hefti, Ph.D.
Proclara Biosciences - Cambridge, MA
Phase 1 Study with NPT088, A Fusion Protein to Treat Alzheimer’s Disease

Mark Tuszyński, M.D.
University of California at San Diego - San Diego, CA
A Clinical Trial of BDNF Gene Therapy in Alzheimer’s Disease

Linda Van Eldik, Ph.D.
University of Kentucky - Lexington, KY
Phase 1b MAD Study of a Novel Drug (MW189) Targeting Neuroinflammation

Manfred Windisch, Ph.D.
Neurokine Therapeutics, LLC - Philadelphia, PA
Phase 1 Study of MW150: Novel Stress Kinase Inhibitor Candidate
Michal Schneider Beeri, Ph.D.
Sheba Medical Center - Ramat Gan, Israel, and Icahn School of Medicine at Mount Sinai - New York, NY
*Intranasal Insulin and Dulaglutide for Cognition in Metabolic Syndrome MCI*

Suzanne Craft, Ph.D.
Wake Forest University Health Sciences - Winston-Salem, NC
*A Phase IIA Trial of Empagliflozin and Intranasal Insulin for MCI/AD*

Stephen Cunnane, Ph.D.
University of Sherbrooke - Quebec, Canada
*Proof of Mechanism of a New Ketogenic Supplement Using Dual Tracer PET*
*Two-time grant winner*

Stephen Cunnane, Ph.D.
University of Sherbrooke - Quebec, Canada
*RCT with a New Ketogenic Salt in MCI*
*Two-time grant winner*

Paul Edison, M.B.B.S, F.R.C.P., Ph.D.
Imperial College London - London, United Kingdom
*Evaluating Oral Semaglutide as a Treatment for Alzheimer’s Disease*
*Two-time grant winner*

Mitchel Kling, M.D.
University of Pennsylvania - Philadelphia, PA
*A biomarker-based trial in MCI/AD*
*Product as tested in this work did not go forward*

Giulio Maria Pasinetti, M.D., Ph.D.
Icahn School of Medicine at Mount Sinai - New York, NY
*BDPP Treatment for Mild Cognitive Impairment and Prediabetes*

Stefano Sensi, M.D., Ph.D.
Università degli Studi Gabriele d’Annunzio di Chieti e Pescara - Chieti, Italy
*Extenzin-Based Therapy for MCI Subjects*

Russell Swerdlow, M.D.
University of Kansas Medical Center - Fairway, KS
*Trial of Oxaloacetate in Alzheimer’s Disease (TOAD) Study*

Part the Cloud propels the global research community and allows it to explore innovative avenues of research that can accelerate needed treatments.”

Maria C. Carrillo, Ph.D.
Chief Science Officer and Medical Affairs Lead, Alzheimer’s Association
Part the Cloud advances research. From more than $65 million in funding PTC has been awarded, grant recipients have gone on to receive more than $1.3 billion in follow-on funding from the U.S. federal government, venture capital firms and other sources.

Follow-On Funding comes from a variety of sources including:
- Foundations (2.3%)
- Private (8.6%)
- Government (32.9%)
- Venture/Corporate (34.4%)
- Indirect (17.5%)

Indirect sources are government, foundation, corporate, venture capital, and individual support that is indirectly related to the Part the Cloud Translational award.

AMYLOID AND TAU

Adam L. Boxer, M.D., Ph.D.**
University of California at San Francisco - San Francisco, CA
Phase I Multiple Ascending Dose Trial of the MT Stabilizer TPI-287 for AD

Dale E. Bredesen, M.D.**
Buck Institute for Research on Aging - Novato, CA
An Exploratory Safety, PK/PD, and Preliminary Efficacy Study of F03 in MCI

Ross Paterson, Ph.D.
Institute of Neurology, University College London - London, United Kingdom
Capturing Tau Kinetics in a Clinical Trial of ASO NI0752 in Alzheimer’s

Tim West, Ph.D.**
C2N Diagnostics – St. Louis, MO
A Single Ascending Dose Double Blinded Placebo Controlled Study of C2N-8E12

Dieter Willbold, Ph.D.
Research Center Juelich GmbH – Jülich, Germany
Placebo Controlled Multi-Ascending Dose [Targeting Protein Aggregation] Phase 1 Study in Healthy Volunteers

**Research studies not advanced
CELL SIGNALING AND COMMUNICATION

Frank Longo, M.D.
Stanford University - Stanford, CA and
Anne Longo
Pharmatrophix, Inc. - Stanford, CA
Phase I Trial for P75 Receptor Ligand

Charbel Moussa, Ph.D.
Georgetown University - Washington, D.C.
Bosutinib Effects on Safety, Biomarkers and Clinical Outcomes in DLB

Paul A. Newhouse, M.D.
Vanderbilt University - Nashville, TN
Phase 1 Testing of a Muscarinic M1 PAM for Alzheimer’s Disease
*Two-time grant winner*

Ahmad Salehi, M.D., Ph.D.
Palo Alto Institute for Research and Education, Inc. - Palo Alto, CA
Improving β2 Adrenergic Signaling in Alzheimer’s Disease

Keith Vossel, M.D., M.Sc
University of California at San Francisco and Gladstone Institute for Neurological Disease - San Francisco, CA
Phase 2a Levetiracetam Trial for AD-Associated Network Hyperexcitability

Nawaf Yassi, M.D., Ph.D.
University of Melbourne - Parkville, Australia
S-Adenosyl Methionine for Alzheimer's Disease

VASCULAR AND OXIDATIVE STRESS

Jan Johansson, M.D., Ph.D.
Artery Therapeutics, Inc. - San Ramon, CA
Human proof of concept of ABCA1 agonist CS6253 treatment

Krista L. Lanctôt, Ph.D.
Sunnybrook Research Institute - Toronto, Canada
Linking GSH and Cognitive Response: A Pilot Phase 2a Study of NAC in VCIND
*Two-time grant winner*

Amala Soumyanath, Ph.D., and Joseph Quinn, M.D.
Oregon Health and Science University - Portland, OR
Safety and Target Engagement of Centella Asiatica in Cognitive Impairment

Whitney Wharton, Ph.D.
Emory University - Atlanta, GA
Mechanistic Potential of Antihypertensives in Preclinical Alzheimer’s
Getting potential treatments faster: propelling high-risk, high-reward research into clinical trials that are aimed at uncovering underlying brain cell changes, timely diagnosis and new treatments for Alzheimer’s and all dementia.

**Research studies not advanced**

**The research trials with this compound did not move forward**

***Moving forward, but not as an AD therapy***

### PRECLINICAL TO PHASE 1a
- VU0467319*
- BDNF
- Pulse Modulation Device
- QIN-100

### PHASE 1a
- CS6253 (ABCA1 agonist)

### PRECLINICAL TO PHASE 1b
- TPI-287*
- F03*
- BDPP Treatment
- Sativex*
- NPT088*
- mGluR5 SAM (BMS-984923)
- XPRO1595

### PHASE 1b
- Centella asiatica
- Intranal Insulin and dulaglutide
- ASO NI0752
- D3D

*Research studies not advanced

**The research trials with this compound did not move forward

***Moving forward, but not as an AD therapy*
**Phase 1 to Phase 2**
- Telmisartan
- Allopregnanolone
- EGCG
- S-Adenosyl Methionine
- Zinc-Sulphate
- Ketone Ester Drink (HVMN Ketone Eser Drink)
- Mesenchymal Stem Cells (Lomecel-B)
- Dasatinib and Quercetin
- BCG Vaccine
- Rapamycin

**Phase 2b**
- Letrozole*
- T3D-959
- Maraviroc
- Valacyclovir
- Transcranial Photobiomodulation (t-PBM)
- IW-6463 (CY6463)**
- Gamma Entrainment Using Sensory Stimuli (GENUS)
- PDE5 Inhibitor
- EI1071
- Empagliflozin and Intranasal Insulin

**Phase 1 to Phase 3**
- NDX-1017 (Drug name changed to ATH1017)
  - Semaglutide

**Phase 3**
- MET-FINGER-APOE (Metformin)
CHALLENGES

Challenges focus on a specific topic and are awarded biennially.

RESCUE AND NEURODEGENERATION

The Part the Cloud to RESCUE (REverse, reStore, Cease and Understand) Brain Cell Degeneration in Alzheimer’s disease challenge aims to accelerate the discovery and testing of innovative compounds to be used for interventions in the earliest stages of neurodegeneration—dementia—Alzheimer’s disease. Presently, there are no effective interventions to delay or prevent the progression of the neurodegenerative processes that underlie the disabling symptoms of Alzheimer’s dementia.

From 45 proposals, six researchers were awarded $1 million each to develop their research over a two-year period.

Roberta Diaz Brinton, Ph.D.
University of Arizona - Tucson, AZ
Advancing Allopregnanolone as a Regenerative Therapeutic for Alzheimer’s

Rafael de la Torre, PharmD, Ph.D.
Institute Mar of Medical Investigations - Barcelona, Spain
Cognitive Decline in Early Stages of AD After EGCG and a Multimodal Therapy

Xue Hua, Ph.D.*
Athira Pharma, Inc. - Seattle, WA
Phase 2a Alzheimer’s Trials of a Novel Neurotrophic Activator, NDX-1017
*No longer an employee of the company; the ongoing trials are overseen by the Athira Leadership Team

Paul A. Newhouse, M.D.**
Vanderbilt University - Nashville, TN
M1-PAM VU319 Effects on Network Connectivity in MCI: A POC Study
*Two-time grant winner*

Stephen M. Strittmatter, M.D., Ph.D.
Yale University - New Haven, CT
Silent Allosteric Modulation of mGluR5 for Alzheimer’s Disease

Raymond Tesi, M.D.
INmune Bio - La Jolla, CA
A Biomarker Directed Study to Reduce Inflammation in Alzheimer’s Disease
NEUROINFLAMMATION

A first-of-its-kind competition, the Part the Cloud Neuroinflammation Challenge was created to accelerate therapeutics and deepen understanding of neurodegeneration to be used in early clinical trials. Scientists around the world were invited to submit proposals that could translate into human trials of treatments targeting neuroinflammation with the goal of improving cognition in individuals with neurodegenerative diseases.

From 60 proposals submitted from 14 countries, four researchers were awarded $1 million each to develop their proposals over a two-year period. After two years, projects were evaluated, and the most outstanding project was awarded an additional $3 million to take it and the field to the next level.

Isidro Ferrer, M.D., Ph.D.**
Center for Networked Biomedical Research on Neurodegenerative Diseases - Barcelona, Spain
Sativex in MCI Patients at High Risk of Developing Alzheimer’s Disease

John M. Olichney, M.D.
University of California at Davis - Davis, CA
Proof of Mechanism Study of Senicapoc in Mild or Prodromal Alzheimer’s Disease

Anthony Andrew Oliva, Ph.D.
Longeveron, LLC - Miami, FL
Clinical Evaluation of Allogenic Mesenchymal Stem Cells for Mild Alzheimer’s Disease
*“After two years, this study was shown to have made the most progress and received this additional award of $3 million.”

Huntington Potter, Ph.D.
University of Colorado at Denver - Denver, CO
Safety & Efficacy of GM-CSF/Leukine in Mild-to-Moderate Alzheimer’s Disease

**“Research studies not advanced”

“This program really knocks innovation out of the ballpark by exploring truly novel mechanisms.”

Paul B. Rosenberg, M.D.
Professor of Psychiatry and Behavioral Sciences at Johns Hopkins University School of Medicine
PART THE CLOUD AND BILL GATES PARTNERSHIP

In 2019, Part the Cloud announced an exciting partnership with Bill Gates, aiming to double our investment in Alzheimer’s research to $60 million. The Alzheimer’s Association, through Part the Cloud, raised over $20 million and, once we reached that mark, Bill Gates provided a $10 million match, allowing us to double our clinical research investment to over $60 million in just one year.

This funding propels high-risk, high-reward research aimed at uncovering underlying brain cell changes, timely diagnosis and new treatments for Alzheimer’s and all dementia. The research grants focus on the following three topic areas:

- **Mitochondria**: how brain cells use energy and fuel (mitochondria, bioenergetics and metabolism)
- **Autophagy / Clearance**: how brain cells remove waste and debris to avoid protein clumping
- **Vascular Contributions**: how blood supply in the brain is maintained

From 128 ideas submitted from 18 countries, over $30 million was awarded to 19 researchers to further develop their research over 3 years.

- **Einor Ben Assayag, Ph.D. and Hen Hallevi, M.D**
  Tel Aviv Sourasky Medical Center - Tel-Aviv, Israel
  *Safety and Efficacy of Maraviroc in Vascular Cognitive Impairment*

- **Anat Biegon, Ph.D.**
  The Research Foundation of SUNY- SUNY at Stony Brook - Stony Brook, NY
  *Aromatase Inhibition in Alzheimer’s Disease: Phase 2 Study*

- **Hung-Kai (Kevin) Chen, M.D., Ph.D.**
  Elixiron Immunotherapeutics Inc. - Taipei, Taiwan
  *CSF1R Inhibitor EI071 for Modulating Microglia-Associated Neuroinflammation*  
  *Two-time grant winner*

- **Davangere P. Devanand, M.D.**
  Research Foundation for Mental Hygiene, Inc. at New York State Psychiatric Institute - New York, NY
  *Anti-Viral Treatment in Mild Cognitive Impairment*

- **David Celermajer, M.D., Ph.D.**
  The Brain Protection Company - Paddington, Australia
  *Phase 1 Study of a Novel Device Reducing Vascular Contributions to Dementia*

- **John Didsbury, Ph.D.**
  T3D Therapeutics, Inc. - Research Triangle Park, NC
  *The PIONEER Study: A Phase 2 Trial of T3D-959 in Alzheimer’s Subjects*
Paul Edison, M.B.B.S, F.R.C.P., Ph.D.  
Imperial College London - London, United Kingdom  
*Mitochondrial Function and BBB Leakage as a Novel Treatment for Alzheimer’s*  
*Two-time grant winner*

Alireza Faridar, M.D.  
The Methodist Hospital Research Institute - Houston, TX  
*Regulatory T cells as a novel therapeutic target in Alzheimer’s Disease*

Nir Grossman, Ph.D.  
Imperial College London - London, United Kingdom  
*Non-Invasive Deep Brain Stimulation for Alzheimer’s Disease*

Dan Iosifescu, M.D.  
New York University School of Medicine - New York, NY  
*Photobiomodulation for Early Stage Alzheimer Disease (PhESAD)*

Miia Kivistö, M.D., Ph.D.  
Imperial College London - London, United Kingdom  
*MET- FINGER- APOE: Multimodal Lifestyle Intervention + Metformin to Prevent Cognitive Decline*

Krista L. Lancôt, Ph.D.  
Sunnybrook Research Institute - Toronto, Canada  
*Exercise as a Primer for Excitatory Stimulation in VCIND (EXPRESS-V)*  
*Two-time grant winner*

Lyndon Lien, Ph.D., M.B.A.  
Qinotto, Inc. - Hillsborough, CA  
*Small molecule lysosome activator for the treatment of neurodegeneration*

Peter Ljubenkov, M.D.  
University of California, San Francisco - San Francisco, CA  
*Veri-T: A phase I Placebo-Controlled Trial of Verdiperstat in FTLD-TDP*

Sudha Seshadri, M.D.  
University of Texas Health Science Center at San Antonio - San Antonio, TX  
*Phase 2 Trial of Rapamycin for Alzheimer’s Disease*

Li-Huei Tsai, Ph.D.  
Massachusetts Institute of Technology - Cambridge, MA  
*Prevention of Alzheimer’s Disease Using Gamma Entrainment*

Chad Glasser, PharmD  
Cyclerion Therapeutics, Inc. - Cambridge, MA  
*Phase 2 Study of CNS sGC Stimulation in AD with Vascular Features*

Thomas Wisniewski, M.D.  
New York University School of Medicine - New York, NY  
*Phase 1 Clinical Trial of Innate Immunity Stimulation via TLR9 in Early AD*

Eti Yoles, Ph.D. and Michal Schwartz, Ph.D.  
ImmunoBrain Checkpoint, Inc. - New York, NY  
*IBC-Ab002 - Immune Checkpoint Blockade to Combat Alzheimer’s Disease*
INTRODUCING THE 2024 PART THE CLOUD GENE TARGETING CHALLENGE

Part the Cloud’s latest funding initiative focuses on personalized medical approaches that address individual genetic circumstances associated with the risk and development of Alzheimer’s.

A number of factors and processes likely contribute to the development of brain diseases such as Alzheimer’s disease, and these may not be the same for every individual.

Scientists have identified more than 100 risk genes associated with the development of Alzheimer’s.

These risk genes may influence biological changes in the brain that differ from person to person, presenting opportunities for personalized gene editing and therapy.

Grants will support new and ongoing early-stage clinical trials using gene targeting. Examples of similar Part the Cloud-funded trials of gene therapies include:

- Ross Paterson, MRCP, Ph.D., University College London, who is conducting a phase 1b trial to test whether targeting specific genes can lead to the reduction of tau tangles.
- Mark Tuszynski, M.D., Ph.D., University of California, San Diego, whose phase 1 gene therapy trial aims to improve the survival and function of brain cells in Alzheimer’s disease.

This Part the Cloud Challenge will supercharge the development of therapies tailored to the genetic underpinnings of Alzheimer’s, accelerating effective treatment for all.

The grant program will enable faster and more focused advancement of these potential therapies into the next stage of development.
THE STAGE IS SET FOR UNPRECEDENTED ACCELERATION OF TARGETED GENETIC RESEARCH FOR ALZHEIMER’S.

WE SEEK VISIONARY PHILANTHROPIC PARTNERS to join with us by making a high-impact gift for this challenge. Together, we will make transformative progress toward our vision of a world without Alzheimer’s and all other dementia.

Learn more and make a donation at ALZ.ORG/PARTTTHECLOUD
FUELING BOLD RESEARCH ACROSS THE GLOBE.

A global research leader, the Alzheimer’s Association is at the forefront of groundbreaking research advancing medical precision in the new era of treatments for Alzheimer’s.

Please consider making a donation to support Part the Cloud and our mission to find a treatment or cure for Alzheimer’s disease in our lifetime.

Learn more and make a donation at ALZ.ORG/PARTTHECLOUD