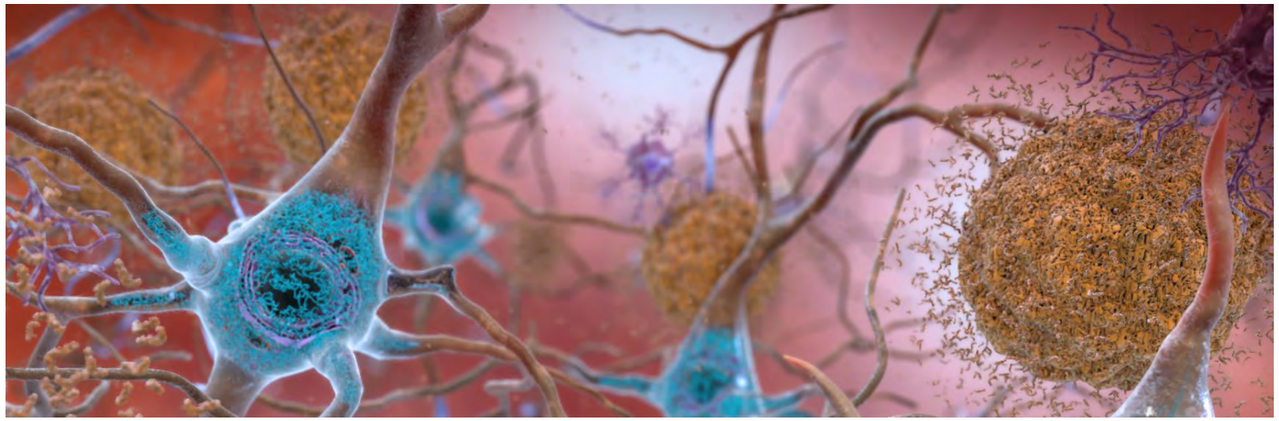


A Path to Prevention: GHR's Alzheimer's Initiative

By 2025, GHR Foundation aims to help develop a therapy to prevent Alzheimer's Disease. Since setting this goal in 2012, GHR has worked with a consortium of government, industry, academic research and other philanthropists to help launch the *first-ever Alzheimer's prevention trials*. GHR continues to track progress in the field, help adjust existing trials, and launch new trials as the science evolves.

GHR's Alzheimer's portfolio is managed by Fred Miller, a Director Emeritus of McKinsey & Company. Miller served McKinsey for more than 27 years and launched their Minneapolis office. He spent his last ten years with the Firm as a leader in their healthcare practice, helping guide business strategy, product development and commercial operations for large healthcare companies. GHR's work is guided by a scientific advisory council.

GHR believes significant recent advances in Alzheimer's research have created the scientific possibility of *preventing Alzheimer's Disease*.

- Advances in brain imaging have made it possible to measure the development of Alzheimer plaques and tangles in the living brain
- Long-term studies have shown the plaques and tangles of Alzheimer's Disease build-up 10-20 years prior to symptom onset
- Advances in genetics can now identify patients at greater risk even before they develop pathology
- New experimental therapies offer the potential to intervene in the disease in a meaningful way for the first time

Scientific Advisory Council

Dr. Maria C. Carrillo, Ph.D.
Chief Science Officer, Medical & Scientific Relations
Alzheimer's Association

Dr. Randall Bateman, M.D.
Charles F. and Joanne Knight Distinguished Professor of Neurology
Washington University School of Medicine

Dr. Ronald C. Petersen, Ph.D., M.D.
Professor of Neurology/Cora Kanow Professor of Alzheimer's Disease Research, Mayo Clinic College of Medicine
Director, Mayo Alzheimer's Disease Research Center

Dr. Reisa Sperling, M.D.
Professor of Neurology, Harvard Medical School
Director, Center for Alzheimer Research and Treatment, Brigham and Women's Hospital and Massachusetts General Hospital Memory Disorders Unit

For more information, visit www.GHRfoundation.org

With a major effort, it should be possible to pull these advances together and bring prevention therapy to the public in this decade.

Finding a way to prevent Alzheimer's Disease is a major undertaking. Prevention projects tend to be long, complex and expensive. In its work, GHR collaborates with a wide range of participants across the field, including: the National Institutes of Health, the National Institute on Aging, Alzheimer's Association, academic research universities, pharmaceutical companies and other philanthropists. In this eco-system, philanthropy often plays the critical role of providing seed money for new projects and flexible funding to adapt to rapid scientific advances.

GHR currently supports four of the leading efforts across the field:

DIAN TU
Dominantly Inherited Alzheimer Network Trials Unit

The Dominantly Inherited Alzheimer's Network (DIAN) is a group of families who carry rare genetic mutations that cause early-onset Alzheimer's Disease. In the DIAN Trials, Dr. Randy Bateman from Washington University is leading research to test a wide range of potential prevention therapies on those families.

Generation Study
ALZHEIMER'S PREVENTION INITIATIVE

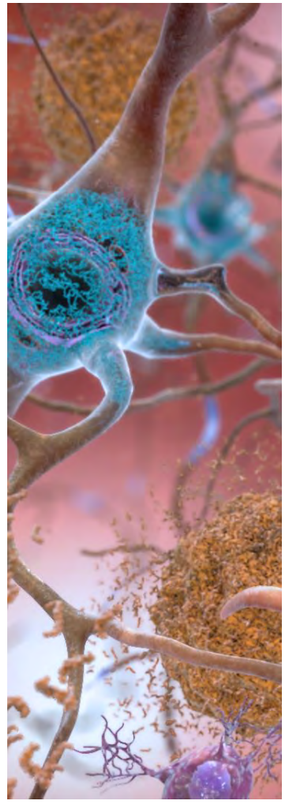
Research led by Dr. Eric Reiman from the Banner Alzheimer's Institute is testing potential prevention therapies in patients at high genetic risk of developing Alzheimer's Disease. This research includes a large-scale genetic screening capability that could be used globally.

The A4 Study
NOW IS THE TIME

Research led by Dr. Reisa Sperling from Harvard University is testing potential plaque screening and prevention therapies for the general population. The lead study in the series is A4—Anti-Amyloid therapy for Asymptomatic Alzheimer's.

MAYO CLINIC
STUDY OF AGING

Led by Dr. Ron Petersen of the Mayo Clinic, this long-term observational study is redefining Alzheimer's Disease by identifying biomarkers that can be used for early diagnosis, long before symptoms emerge.



GHR FOUNDATION®

Progress

GHR's partners have made remarkable progress since launching the initiative in 2012.

- The DIAN trial was launched in 2013 as the first-ever Alzheimer's prevention trial. The first wave results are expected in early 2020
- The A4 trial was launched in 2014 as the first-ever Alzheimer's prevention trial for the general population; this trial is fully enrolled and on track for completion in 2022
- The Generation trial was launched in 2015 to test a large-scale genetic screening and prevention program; to date, more than 55,000 people have volunteered for screening and have been genetically tested
- A second wave of the DIAN trial was launched in 2016 to test new experimental therapies that recently became available
- The A4 trial protocol was modified in 2017 with endorsement by the National Institute on Aging and approval by the FDA to reflect recent learning from the field and improve the odds of success
- The Mayo Clinic Study of Aging has contributed to a new research framework adopted by the National Institute of Aging in 2018; the framework fundamentally defines Alzheimer's Disease based on its underlying pathology rather than symptoms

Our Strategy

1. Fully investigate the use of experimental anti-plaque drugs as prevention therapy, with future trials testing:
   a. Earlier interventions
   b. More potent therapies
   c. Combination therapies
2. Monitor the progress of experimental drugs for new targets, such as tangles and inflammation.
3. Support transition from symptomatic to pathologic diagnosis

2012	2013	2014	2015	2016	2017	2018	2020	2022	2024	2025
Alzheimer's Initiative launched	DIAN trial launched	A4 trial launched	Generation Study launched	DIAN second wave launched	A4 trial protocol modified	Mayo research framework adopted by NIH	DIAN results expected	A4 results expected	Generation Study results expected	Goal for prevention therapy