

Treating Alzheimer's: A New Era Begins with Lecanemab

Few diagnoses in medicine are more devastating than Alzheimer's disease (AD). Barely known to the public four decades ago, the number of people living with dementia – estimated to stand at 55 million in 2019 – is expected to rise to 139 million in 2050¹, and 75% of these individuals have not been diagnosed. The toll on patients, families, and society of this ubiquitous and ultimately fatal disorder is staggering. The number affected more than doubles if one includes the millions of cognitively normal older people who do not yet know the disease is underway in their brains. But breaking news from the Clinical Trials in Alzheimer's Disease (CTAD) Conference late November 2022 suggests this bleak outlook is changing. A disease-modifying treatment for Alzheimer's has finished a highly successful trial (called Clarity AD), the results of which will soon be reviewed by the U.S Food and Drug Administration, with approval widely expected to follow.

At the CTAD Conference in San Francisco, around 2000 physicians, scientists, pharmaceutical investigators and others viewed and intensively discussed the Clarity AD findings². The data presentations were detailed, comprehensive, and transparent. Most AD experts in the audience responded with enthusiastic approval, viewing this study of lecanemab, a monoclonal antibody which preferentially targets Abeta "protofibrils" (smaller Abeta assemblies), as the most clearly positive and encouraging AD trial yet completed. In this randomized, double-blinded, placebo-controlled trial of 1,795 patients with mild cognitive impairment (MCI) or mild AD dementia, intravenous lecanemab given every two weeks over 18 months led to statistically significant ($p < 0.001$) slowing of cognitive and functional decline on the CDR-SB primary outcome and on all three secondary outcomes related to cognition and daily function (ADAS-cog14; ADCOMS; ADCS-MCI score on Activities of Daily Living). Sensitivity analyses showed similar effects, indicating the robustness of the study results. On average, the slowing of decline on the key endpoints ranged from 23% to 37% vs. placebo. Importantly, these meaningful effects of lecanemab over placebo widened from 3 to 18 months of treatment on all 5 key outcomes, signifying clinical benefit and providing a rational basis for hoping that even more slowing will occur over time. There were also sizeable and significant positive effects on classical biological markers of AD: amyloid plaques and neurofibrillary tangles on PET scans and blood and spinal fluid levels of the proteins that comprise these hallmark lesions of AD. Thus, lecanemab appears to reduce amyloid pathology in AD and beneficially slows the cascade of biological events which result in cognitive decline.

Throughout the meeting, clinicians who have collectively cared for millions of Alzheimer's patients and families referred to this outcome as a foundational gamechanger in a disease which inexorably robs its victims of their most human qualities -- memory, judgment, equanimity, and independence (the conduct of everyday life). The results presented at CTAD suggest that over the course of the 18-month trial, those on lecanemab progressed almost 6 months slower than those on placebo. Treatments like lecanemab hold the promise of improving the quality of life of our patients and their families experiencing AD. Indeed, evidence of such benefits were observed in the form of 25-50% less decline on four scales of patient- and caregiver-reported quality of life and disease burden.

Regarding safety, the key adverse event, as expected, was the development of amyloid-related imaging abnormalities (ARIA) seen on MRI scans. ARIA with localized, typically transient brain edema (ARIA-E) occurred in 12.6% of lecanemab recipients and 1.7% of those on placebo overall. Less than 3% of patients had any symptoms associated with ARIA, and serious symptoms were even more rare. The

ARIA-E rate was lower than in previous trials of antibodies that target amyloid plaques directly. ARIA was well managed in the trial, with careful safety monitoring by knowledgeable clinicians. Other adverse events included infusion-related reactions occurring during the first infusion and not interfering with continued treatment. For appropriately selected patients under the care of proficient clinicians with sufficient resources to provide proper patient detection and monitoring, ARIA risk should be manageable in real-world clinical settings. The longer-term safety and efficacy of lecanemab in actual practice can be monitored in longitudinal registries, such as the recently launched Alzheimer's Network (ALZNET).

The Clarity AD trial represents an unprecedented and foundational leap in the search for a disease-modifying treatment for AD. It is the first to show an unequivocal effect in changing the rate of decline on diverse clinical, cognitive, and functional endpoints, converging with validated, AD-associated brain, cerebrospinal fluid and blood biomarker endpoints. Further success may be possible with this treatment as we leverage biomarker-informed precision medicine approaches that should increase treatment benefits and reduce risk and burdens in subsets of AD patients.

The success of lecanemab is not a reason to pause our efforts or interrupt the momentum towards better treatments for AD. Lecanemab is not a cure for AD. Over months and years, treated patients will continue to decline but, on average, would be expected to do so more slowly. Some are likely to benefit more than others, as in all chronic diseases. Our patients will need ever more effective therapies, and their families need the hope and relief that these treatments will provide. The Clarity AD results will spur more investment in Alzheimer diagnostics and therapeutics. Non-pharmacological approaches that seek to reduce lifestyle factors or therapeutics that address other AD-associated pathways can be combined with this new medicine.

Yet even as we continue to work to push our field forward, we must get scientifically validated and clinically relevant therapies like lecanemab to patients as soon as possible. Lecanemab was developed and tested in patients with early-stage AD, and every day of delay in patient access to this therapy may result in treatable patients progressing beyond the window of therapeutic opportunity. We cannot allow the uninterrupted decline of AD patients we have known for decades to continue when effective therapies are available.

The many undersigned AD clinicians and other experts know this terrible disease all too well from witnessing it up close. We herald the foundational advance represented by the advent of lecanemab therapy. Now, we must build on the success of science to translate these gains into even better outcomes for patients and families. Autonomy and justice dictate that our patients have equitable access and the opportunity to make informed choices regarding reasonable treatments that can impact their lives and well-being. No barrier can be allowed to stand between our patients and a treatment that has a reasonable risk-benefit ratio and significantly reduces the causative pathology.

1. World Health Organization, <https://www.who.int/news-room/fact-sheets/detail/dementia>, last accessed 12/7/2022
2. van Dyck, Christopher H et al. "Lecanemab in Early Alzheimer's Disease." *The New England journal of medicine*, 10.1056/NEJMoa2212948. 29 Nov. 2022, doi:10.1056/NEJMoa2212948

SIGNEES:

Paul Aisen, MD
Alzheimer's Therapeutic
Research Institute,
University of Southern
California

**Ricardo F. Allegri, MD, PhD,
FAAN**
Instituto Neurológico Fleni,
Buenos Aires, Argentina

Michael L. Alosco, PhD
Boston University Chobanian &
Avedisian School of Medicine

**Allan A. Anderson, MD,
MMM**
Banner Alzheimer's Institute in
Tucson

**Liana G. Apostolova, MD,
MSc, FAAN**
Indiana University

Igor Pruber Q C Araujo, MD
UCSF

Nicholas Ashton, PhD
University of Gothenburg

Alireza Atri, MD, PhD
Banner Sun Health Research
Institute

Walter Baehr, MD
University of Alabama at
Birmingham

Suzanne L. Baker, PhD
Lawrence Berkeley National
Lab

Henryk Barthel, MD
Leipzig University Medical
Center

Randall J. Bateman, MD
Washington University School
of Medicine

Luis I. Becerra, MD
Nova Southeastern University

Maryam Beigi, MD
UCLA

**Tammie L. S. Benzinger, MD,
PhD**
Washington University

Bradley F. Boeve, MD
Mayo Clinic

Malaz Boustani, MD, MPH
Indiana University

Femke Bouwman, MD, PhD
Alzheimer Centre Amsterdam
UMC

Adam Boxer, MD, PhD
UCSF

Noa Bregman, MD
Tel Aviv Medical Center

Jared R. Brosch, MD
Indiana University

Christine J. Cliatt Brown, MD
University of Utah

Jesse Brown, PhD
UCSF

Anna D. Burke, MD
Barrow Neurological Institute

Oleg Butovsky, PhD
Brigham and Women's
Hospital, Harvard Medical
School

Ismael L. Calandri, MD
Fleni

**Cynthia M. Carlsson, MD,
MS**
University of Wisconsin School
of Medicine and Public Health

Kaitlin Casaletto, PhD
UCSF

Frédéric Checler, PhD
CNRS

David G. Clark, MD
Indiana University

Ann Cohen, PhD
University of Pittsburgh School
of Medicine

Scott E. Counts, PhD
Michigan State University

Jon Cross, MD
Visionary Investigators
Network

Jeffrey Cummings, MD, ScD
University of Nevada Las Vegas

Kirk R Daffner, MD
Brigham and Women's
Hospital/Harvard Medical
School

Steven T. DeKosky, MD
Alzheimer's Disease Research
Center, University of Florida

Ulf Dettmer, PhD
Brigham and Women's Hospital

Michael C. Donohue, PhD
Alzheimer's Therapeutic
Research Institute, University of
Southern California

Ranjan Duara, MD
1 Florida ADRC, University of
Florida College of Medicine

Linda J. Van Eldik, PhD
University of Kentucky

**Nilufer Ertekin-Taner, MD,
PhD**
Mayo Clinic Florida

Martin Farlow, MD
Indiana University School of
Medicine

Wiesje van der Flier
Amsterdam UMC

Concetta Forchetti, MD, PhD
Northwestern University

Tatiana Foroud, PhD
Indiana University School of
Medicine

Norman L. Foster, MD
University of Utah

Nicole R. Fowler, PhD, MHSA
Indiana University

Nick C. Fox
UCL

Giovanni Frisoni, MD
Geneva University Hospital

Nicholas A. Frost, MD, PhD
University of Utah

Douglas Galasko, MD
University of California, San
Diego

Seth Gale, MD
Brigham and Women's
Hospital, Harvard Medical
School

Yonas E. Geda, MD
Barrow Neurological Institute

David S. Geldmacher, MD
University of Alabama at
Birmingham

Todd E. Golde, MD, PhD
Emory University

Danielle Goldfarb, MD
Banner Sun Health Research
Institute

**Mark A. Goldstein MD,
FAAN**
JEM/Headlands Research

Cheng-Xin Gong, MD
New York State Institute for
Basic Research in
Developmental Disabilities

Marcia N. Gordon, PhD
Michigan State University

Jürgen Götz, PhD
University of Queensland
(Australia)

Joshua Grill, PhD
University of California, Irvine

**Lea Tenenholz Grinberg, MD,
PhD**
University of California, San
Francisco

Christian Haass
Ludwig Maximilians University
Munich

**Dustin B. Hammers, PhD,
ABPP-CN**
Indiana University

Oskar Hansson, MD, PhD
Lund University

Suzanne B. Hendrix, PhD
Pentara

Doris Molina Henry, PhD
University of Southern
California

Vered Hermush, MD
Laniado Medical Center, Ariel
University Israel

Annie Hiniker, MD, PhD
University of California, San
Diego

**Brandon Blake Holmes, MD,
PhD**
University of California San
Francisco

David M. Holtzman, MD
Washington University in St.
Louis

**Lawrence S. Honig, MD, PhD,
FAAN**
Columbia University Irving
Medical Center, New York, NY

Khalid Iqbal, PhD
New York State Institute for
Basic Research in
Developmental Disabilities and
City University of New York

Atsushi Iwata, MD, PhD
Tokyo Metropolitan Geriatric
Institute

William Jagust, MD
University of California
Berkeley

Gregory A. Jicha
University of Kentucky

Charles Jennings, PhD
Brigham and Women's Hospital

Kimball A. Johnson, MD
CenExel iResearch Atlanta
Medical Director

Sterling Johnson, PhD
University of Wisconsin-
Madison

Parunyou Julayanont, MD
Barrow Neurological Institute

Kejal Kantarci, MD, MS
Mayo Clinic

Anumantha Kanthasamy
University of Georgia

Jason Karlawish, MD
University of Pennsylvania

Diana R. Kerwin, MD
Kerwin Medical Center

Vikram Khurana, MD, PhD
Harvard Medical School and
Brigham and Women's Hospital

Hee Jin Kim
Samsung Medical Center

William E. Klunk, MD, PhD
University of Pittsburgh

David S. Knopman, MD
Mayo Clinic, Rochester MN

Rada Koldamova, MD, PhD
University of Pittsburgh

Joel Kramer, PsyD
UCSF

Sarah Kremen, MD
Cedars-Sinai

Walter A. Kukull, PhD
University of Washington;
National Alzheimer's
Coordinating Center (NACC)

Robert Laforce, MD, PhD
CHU de Québec, Université
Laval, Québec, Canada

Debomoy K. Lahiri, PhD,
FAAAS
Indiana University School of
Medicine

Bruce Lamb, PhD
Indiana University School of
Medicine

Susan Landau, PhD
UC Berkeley

Edward B. Lee, MD, PhD
University of Pennsylvania

Suzee E. Lee, MD
University of California, San
Francisco

Iliya Lefterov, MD, PhD
University of Pittsburgh

Cynthia A Lemere, PhD
Brigham and Women's Hospital,
Harvard Medical School

Allan I. Levey, MD, PhD
Emory Goizueta Alzheimer's
Disease Research Center

Stefan Lichtenthaler, PhD
DZNE (German Center for
Neurodegenerative Diseases)

Spencer W. Liebel, PhD
University of Utah

Lei Liu, MD, PhD
Brigham and Women's Hospital

Peter A. Ljubenkov, MD
University of California, San
Francisco, Memory and Aging
Center, Weill Institute for
Neurosciences

Justin M. Long, MD, PhD
Washington University in St
Louis

Marissa Natelson Love, MD
University of Alabama at
Birmingham

Val J. Lowe, MD
Mayo Clinic

Yvonne Lu, PhD, RN, FGSA,
FAAN
Indiana University School of
Nursing

Joseph C. Masdeu, MD, PhD
Nantz National Alzheimer
Center, Houston Methodist, and
Weill Cornell Medicine

Gad A. Marshall, MD
Brigham and Women's Hospital

Colin L. Masters
The Florey Institute,
The University of Melbourne

Eric McDade, DO
Washington University

Amy McLean, DNP
Barrow Neurological Institute

Scott M. McGinnis, MD
Brigham & Women's Hospital

Michael B. Miller, MD, PhD
Brigham and Women's Hospital,
Harvard Medical School

David G. Morgan, PhD
Michigan State University

John C. Morris, MD
Washington University in St
Louis

Richard G. M. Morris
The University of Edinburgh

Beth Mormino, PhD
Stanford

Cath Mummery, MD, PhD
University College London

Melissa E. Murray, PhD
Mayo Clinic Florida

Salvatore Napoli
Neurology Center of New
England

Peter T. Nelson, MD, PhD
University of Kentucky

Aivi T. Nguyen, MD
Mayo Clinic

Adrian L. Oblak, PhD
Indiana University School of
Medicine

Kenjiro Ono, PhD, MD
Kanazawa University

Rik Ossenkoppele, PhD
Amsterdam University Medical
Centers / Lund University

Emily Paolillo, PhD
UCSF Memory and Aging
Center

Mike Pappolla, MD, PhD
University of Texas Medical
Branch

Victoria S. Pelak, MD
University of Colorado School
of Medicine

Ronald Petersen, PhD, MD
Mayo Clinic

Peter S. Pressman
University of Colorado,
Anschutz Medical Campus

**Gil D. Rabinovici, MD,
FAAN, FANA**
University of California San
Francisco

Rema Raman, PhD
Alzheimer's Therapeutic
Research Institute, Keck School
of Medicine, University of
Southern California

Vijay K Ramanan, MD, PhD
Mayo Clinic

Kamalini Ranasinghe
UCSF

Katherine P. Rankin, PhD
University of California San
Francisco

P. Hemachandra Reddy, PhD
Texas Tech University Health
Sciences Center

R. Ross Reichard
Mayo Clinic

Ashley Reiff LCSW
Indiana University

Dorene M. Rentz, PsyD
Brigham and Women's Hospital
Harvard Medical School

Robert Rissman, PhD
University of Southern
California

Erik Roberson, MD, PhD
University of Alabama at
Birmingham

Julio C. Rojas, MD, PhD
Memory and Aging Center,
University of California, San
Francisco

Howard Rosen, MD
University of California, San
Francisco

Owen A. Ross, PhD
Mayo Clinic

**Christopher C. Rowe, BMBS,
MD, FRACP**
University of Melbourne

**Marwan Noel Sabbagh MD,
FAAN**
Barrow Neurological Institute

Carl Sadowsky, MD
Palm Beach Neurology

S Ahmad Sajjadi, MD, PhD
University of California Irvine

Stephen Salloway, MD, MS
Memory & Aging, Butler
Hospital and the Warren Alpert
Medical School of Brown
University

Rowan Saloner, PhD
University of California, San
Francisco

Kumar Sambamurti, PhD
Medical University of South
Carolina

Andrew J. Saykin, PsyD
Indiana ADRC, Indiana
University School of Medicine

**Prof. Philip Scheltens, MD,
PhD**
Alzheimer Center Amsterdam
University Medical Center

Julie Schneider
Rush Alzheimer's Disease
Center

Michael Schöll, PhD
University of Gothenburg

Professor Jonathan M. Schott, MD, FRCP, FAAN
University College London, UK

Julie Schwartzbard
Aventura Neurologic Associates

Dennis Selkoe, MD
Harvard Medical School,
Brigham and Women's Hospital

Sharon J. Sha, MD, MS
Stanford University

Leslie M. Shaw, PhD
Perelman School of Medicine,
University of Pennsylvania

Eric Siemers, MD
Siemers Integration LLC

Bryan Luke Smesler
University of Alabama in
Birmingham

Amanda G. Smith, MD
USF Health Byrd Alzheimer's
Institute

B. Joy Snider, MD, PhD
Knight Alzheimer Disease
Research Center, Washington
University School of Medicine

Peter J. Snyder, PhD
The University of Rhode Island

Deborah Sokol, PhD, MD,
ABCN
IUPUI

Weihong Song
Institute of Aging, Wenzhou
Medical University

Michelle Sorweid, DO, MPH
University of Utah

Reisa Sperling, MD
Mass General Brigham, Harvard
Medical School

Salvatore Spina, MD, PhD
University of California San
Francisco

Adam M. Staffaroni, PhD
University of California, San
Francisco

Susan Steen, MD
Axiom Clinical Research of
Florida

Andrew Stern, MD, PhD
Brigham and Women's Hospital

David Tanne
Rambam Health Care Campus,
Haifa, Israel

Malu G. Tansey, PhD
University of Florida

Carmela Tartaglia
University Health Network

Boon Lead Tee, MD
University of California, San
Francisco

Marilù Gorno Tempini, MD,
PhD
UCSF

David B. Teplow, PhD
David Geffen School of
Medicine at UCLA

Mahendra Kumar Thakur
Banaras Hindu University, India

Paul M. Thompson, PhD
Stevens Neuroimaging Institute,
Keck School of Medicine,
University of Southern
California

Lars Olof Tjebberg, PhD
Karolinska Institutet

Taisuke Tomita, PhD
The University of Tokyo

Elena Tsoy, PhD
University of California San
Francisco

Raymond Scott Turner
Georgetown University

Lawren VandeVrede, MD,
PhD
UCSF Alzheimer's Disease
Research Center

Robert Vassar, PhD
Feinberg School of Medicine,
Northwestern University

Prashanthi Vemuri, PhD
Mayo Clinic

Everard (Jort) Vijverberg,
PhD, MD
Amsterdam UMC/Alzheimer
Center Amsterdam

Qing Wang, PhD
Washington University School
of Medicine

Ruizhi Wang
Indiana University

David Weisman
Abington Neurological
Associates

Alexander White, MD
Progressive Medical Research

Meredith Wicklund, MD
Mayo Clinic Arizona

Michael W. Weiner, MD
University of California, San
Francisco

Donna M. Wilcock, PhD
University of Kentucky
Sanders-Brown Center on
Aging

Charles Windon, MD
UCSF

David A. Wolk, MD
Penn Alzheimer's Disease
Research Center

Benjamin Wolozin, MD, PhD
Boston University School of
Medicine

Bryan Woodruff, MD
Mayo Clinic Arizona

Pauline Wu, DO
UCLA

**Heather Wynne-Phillips,
MSN, APRN, FNP-C**
USF Health Byrd Alzheimer's
Institute

Hyun-Sik Yang, MD
Brigham and Women's Hospital

Keir Yong, PhD
UCL

Tracy Young-Pearse, PhD
Brigham and Women's Hospital,
Harvard Medical School

Ehud Zeltzer, MD
University of California, San
Francisco

Henrik Zetterberg, MD, PhD
University of Gothenburg

Vered Hermush, MD
Ariel University, Sanz Medical
Center, Netanya, Israel

Takaomi C. Suido, PhD

RIKEN Center for Brain
Science

Takeshi Iwatsubo, MD
The University of Tokyo

Barry D. Greenberg, PhD
Johns Hopkins University
School of Medicine

**Stephanie De Santiago, DNP,
AGNP-C**
Banner Sun Health Research
Institute

CONFLICT OF INTEREST DISCLOSURES
(declared by signees)

Paul Aisen, MD

Dr. Aisen has research agreements with Eisai and Lilly, and has consulted with Merck, Biogen, Genentech, Roche and Abbvie

Ricardo F. Allegri

None

Michael L. Alosco, PhD

None

**Allan A. Anderson, MD,
MMM**

None

**Liana G. Apostolova, MD,
MSc, FAAN**

Dr. Apostolova has served as a consultant for both Eisai and Biogen

Igor Prufer Q C Araujo, MD

Minor amount of shares with Biogen

Nicholas Ashton, PhD

None

Alireza Atri, MD, PhD

Dr. Atri discloses that over the last 20+ years as a practicing cognitive neurologist, neuroscientist and AD clinical trialist he has served as an investigator or consultant for many organizations (public, private, foundation, governmental and non-profits) and bio-pharmaceutical companies, including multiple biopharmaceutical companies that have AD-related or anti-amyloid monoclonal antibodies experimental therapeutics, drugs or pipelines. Directly relevant to

this statement on lecanemab, Dr. Atri specifically discloses that he has consulted or served as a site-investigator on sponsored trials to his institution for the collaborating partners and makers of lecanemab: Eisai and Biogen. The views expressed by signing this letter on lecanemab are his own.

Walter Baehr, MD

None

Suzanne L Baker, PhD

Consults for Genentech

Henryk Barthel, MD

None

Randall J. Bateman, MD

Alzheimer's Association Zenith Grant, American Health Assistance Foundation, Glenn Foundation, Ruth K. Broad Biomedical Research Foundation, Anonymous Foundation, Merck research collaboration. Alzheimer's Association, Association for Frontotemporal Degeneration FTD Biomarkers Initiative, BrightFocus Foundation, Cure Alzheimer's Fund, Foundation for Barnes Jewish Hospital, GHR Foundation, MetLife Foundation, Rainwater Foundation Tau Consortium, Tau SILK Consortium (Abbvie, Biogen, Lilly), Centene, Stable Isotope Labeling Quantitation (SILQ) Center donors Richard Frimel, David & Amy Payne, John & Linda Tracy, Pat and Jane Tracy, Tom & Catherine Tracy, Robert Willman, NfL

Consortium (Abbvie, Biogen, Roche, UCL, BMS).

DIAN-TU Pharma Consortium: (Active: Biogen, Eisai, Eli Lilly & Co., Janssen, Roche/Genentech, United Neuroscience. Previous: AbbVie, Amgen, AstraZeneca, Forum, Mithridion, Novartis, Pfizer, Sanofi)

DIAN-TU Trial Companies: Eisai, Eli Lilly and Co., Roche, Janssen, Avid Radiopharmaceuticals
Invited Speaker (12 months): Roche, Novartis, USC

Consulting Relationships (12 months): AC Immune, Eisai, Roche

Randall J Bateman is a co-founder and on the scientific advisory board of C2N Diagnostics and reports research support from AbbVie, Avid Radiopharmaceuticals, Biogen, Bristol Meyers Squibb, Centene, Eisai, Eli Lilly and Company, Genentech, Inc., F. Hoffmann-La Roche Ltd, Janssen, and Novartis. He has provided consulting services for Amgen and F. Hoffman La-Roche. Washington University has equity ownership interest in C2N Diagnostics.

Luis I. Becerra, MD

None

Maryam Beigi, MD

None

Tammie L. S. Benzinger, MD, PhD

Consultant for Biogen, Eisai, Roche, Lilly, Avid Radiopharmaceuticals Siemens

Bradley F. Boeve, MD

Institutional research grant support for clinical trials sponsored by Alector, Biogen, Transposon, Cognition Therapeutics, GE Healthcare.

Malaz Boustani, MD, MPH

Serves as a consultant and advisory board member for Eisai, Biogen, Genentech, Lilly, Acadia, and Merck. Founded the following companies: PPHM, LLC, RestUp, LLC, BlueAgilis, Inc, and DigiCare Realized, Inc.

Femke Bouwman, MD, PhD

Biogen, Roche, Optina Dx, Optos

Adam Boxer

Site PI for Clarity

Noa Bregman, MD

None

Jared R. Brosch, MD

Participated in the clinical trials for Lecanemab and Indiana University has received compensation from Biogen/Eisai in order to facilitate these studies.

Christine J. Cliatt Brown, MD

None

Jesse Brown, PhD

None

Anna D. Burke, MD

Consultant for Biogen, Eisai, Roche, Lilly, Acadia

Oleg Butovsky, PhD

None

Ismael L. Calandri, MD

None

Cynthia M. Carlsson, MD, MS

Dr. Carlsson receives grant funding from the National Institute on Aging, the Department of Veterans Affairs, and serves as site principal investigator for the AHEAD Study (Eisai/NIH) and the A4 Study (Lilly/NIH).

Kaitlin Casaletto, PhD

None

Frédéric Checler

None

David G. Clark, MD

None

Ann Cohen, PhD

None

Scott E. Counts, PhD

None

Jon Cross, MD

None

Jeffrey Cummings

None

Kirk R Daffner, MD

None

Steven T. DeKosky, MD

Chairs DSMBs for Biogen, Vaccinex, and Prevail Pharmaceuticals, serves on a medical advisory boards for Cognition Therapeutics, and is an editor for dementia for UpToDate, a point of care medical text.

Ulf Dettmer, PhD

None

Michael C. Donohue, PhD

Dr. Donohue consulted for Roche, received research funding from Eli Lilly and Eisai, and his spouse is a full-time employee of Janssen.

Ranjan Duara, MD

None

Linda J. Van Eldik, PhD

None

Nilufer Ertekin-Taner, MD, PhD

None

Martin Farlow

None

Wiesje van der Flier

WF has performed contract research for Biogen MA Inc, and Boehringer Ingelheim. WF has been an invited speaker at Boehringer Ingelheim, Biogen MA Inc, Danone, Eisai, WebMD Neurology (Medscape), NovoNordisk, Springer Healthcare, European Brain Council. WF is consultant to Oxford Health Policy Forum CIC, Roche, and Biogen MA Inc. WF participated in advisory boards of Biogen MA Inc, Roche, and Eli Lilly. All funding is paid to her institution.

WF is member of the steering committee of PAVE, and Think Brain Health.

WF was associate editor of Alzheimer, Research & Therapy in 2020/2021. WF is associate editor at Brain.

Concetta Forchetti, MD, PhD

I do not own stock and do not benefit from the profit of EISAI/Biogen companies. I have given educational presentations in the past for which I am compensated.

Tatiana Foroud, PhD

None

Norman L. Foster, MD

Site principal investigator for aducanumab clinical trial sponsored by Biogen

Nicole R. Fowler, PhD, MHSA

None

Nick C. Fox

I have served on advisory boards for clinical trials or provided consultancy for Biogen, Ionis, Lilly and Roche - payments have been to my institution (UCL) rather than to me personally.

Giovanni Frisoni, MD

No competing interest with Eisai. I received compensations for consultancies from Biogen - among others.

Nicholas A. Frost, MD, PhD

None

Douglas Galasko, MD

Paid consultant to Biogen, Eisai, Fujirebio.

Seth Gale, MD

I am a Site PI for the CLARITY AD study

Yonas E. Geda, MD

None

David S. Geldmacher, MD

I have received research funding (paid to my institution) and consulting fees (paid to me) related to this class of therapy from Biogen, Eisai, and Genentech, as well as consulting fees (paid to me) by Lilly.

Todd E. Golde, MD, PhD

None

Danielle Goldfarb, MD

I served on an Alzheimer's advisory board for Eisai.

Mark A. Goldstein MD,**FAAN**

None

Cheng-Xin Gong, MD

None

Marcia N. Gordon, PhD

None

Jürgen Götz, PhD

None

Joshua Grill, PhD

Received research support but not direct financial compensation from Eisai.

Lea Tenenholz Grinberg MD, PhD

I receive research funding from the Alzheimer's Association, Rainwater Charity Foundation and Weill Neuroscience Institute. I am a part of the Alzheimer's Association Medical and Scientific Advisory Board.

Christian Haass

I collaborate with Denali Therapeutics on microglial modulating antibodies. I am chief advisor of ISAR

Bioscience and a member of the advisory board of AviadoBio.

Dustin B. Hammers, PhD, ABPP-CN

None

Oskar Hansson, MD, PhD

OH has acquired research support (for the institution) from ADx, AVID Radiopharmaceuticals, Biogen, Eli Lilly, Eisai, Fujirebio, GE Healthcare, Pfizer, and Roche. In the past 2 years, he has received consultancy/speaker fees from AC Immune, Amylyx, Alzpath, BioArctic, Biogen, Cerveau, Eisai, Fujirebio, Genentech, Novartis, Novo Nordisk, Roche, and Siemens.

Suzanne B Hendrix, PhD

On Eisai's global advisory committee, advisor to Biogen, Lilly and many other companies in the AD field.

Doris Molina Henry, PhD

Doris Molina Henry has received funding from American Heart Association and Eisai for the AHEAD 3-45 studies (as a public-private partnership). She is an unpaid member of the Alz IRGP Council for the Alzheimer's Association. Dr. Molina Henry was not involved in the CLARITY-AD trial.

Vered Hermush, MD

None

Annie Hiniker, MD, PhD

None

Brandon Blake Holmes, MD, PhD

None

David M. Holtzman, MD
Co-founder, with equity, C2N Diagnostics LLC. Scientific advisory boards/consulting: Genentech, Denali, C2N Diagnostics, Cajal Neurosciences, Alector. DMH is an inventor on a 1) a patent licensed by Washington University to NextCure on anti-apoE antibodies, 2) a patent licensed by Washington University to Eli Lilly on a humanized anti-A β antibody, 3) a patent licensed by Washington University to C2N Diagnostics on a humanized anti-tau antibody.

Lawrence S. Honig, MD, PhD, FAAN
Consultant for Biogen, Cortexyme, Eisai, Genentech, Medscape, Prevail, Roche. Recent research funding from Abbvie, Acumen, Alector, Biogen, Eisai, Genentech, Janssen, Eli Lilly, Roche, UCB, Transposon, Vaccinex.

Khalid Iqbal, PhD
Chief Scientific Officer of Phanes Biotech, which is carrying out drug discovery studies on immunotherapy targeting tau and Abeta pathologies and on neural regeneration that can prevent both tau and Abeta pathologies.

Atsushi Iwata, MD, PhD
I am a member of Eisai Global Advisory board

William Jagust, MD
Has consulted for Lilly, Eisai, Biogen, and Bioclinica

Gregory A. Jicha
Received compensation from Eisai for contract research activities in the Phase 2 study. CLARITY Phase 3, and the A345 AHEAD study.

Charles Jennings, PhD
Spouse is an employee of Prime Medicine, a biotech company that develops clinical applications of genome editing technologies.

Kimball A. Johnson, MD
Principal Investigator for Eisai Study @ CenExel iResearch Atlanta

Sterling Johnson, PhD
SCJ has served as a consultant to Roche, Eisai and Prothena in the past three years.

Parunyou Julayanont, MD
None

Kejal Kantarci, MD, MS
Receives research support from Avid Radiopharmaceuticals, Eli Lilly and is a paid consultant for Biogen

Anumantha Kanthasamy
Have two startup companies: PK Biosciences, Inc. and Probiome Therapeutics. The work performed in the startup companies is unrelated to this publication.

Jason Karlawish, MD
None

Diana R. Kerwin, MD
I am a site principal investigator for the CLARITY study, blinded to study data.

Vikram Khurana, MD, PhD
None

Hee Jin Kim
None

William E. Klunk, MD, PhD
None

David S. Knopman, MD
I am a site investigator in the EMBARK study (Biogen) and in the A4 (Lilly) but receive no personal compensation. I attended a meeting on Dec 2, 2022 with Eisai regarding lecanemab but received no personal compensation.

Rada Koldamova, MD, PhD
None

Joel Kramer, PsyD
None

Sarah Kremen, MD
Was a site PI for Biogen PRIME and ENGAGE studies and consultant for ICER's review of aducanumab, and has served on an advisory board for Eli Lilly.

Walter A. Kukull, PhD
I have grant support from NIH/NIA.

Robert Laforce, MD, PhD
None

Debomoy K. Lahiri, PhD, FAAAS
Dr. Lahiri acknowledges the support from the NIH, NIA (R01AG051086, R56AG072810, R21AG076202, R21AG AG074539, P30AG10133, and P01AG014449), and also from Bentham Science Publications

(as Editor-in-Chief, Current Alzheimer Research, and Current Aging Science). He has stock options in Annovis Bio, Inc, and serves as Chief Scientific Advisor, Peptide Therapeutics Provoidya, Indianapolis.

Bruce Lamb, PhD

Consultant for NervGen Inc., leader of multiple NIH-funded research programs, volunteer advisor as Chair of the Medical and Scientific Advisory Group (MSAG) of the Alzheimer's Association.

Susan Landau, PhD

I serve on a DSMB for KeifeRX and have received speaking honoraria from Eisai

Edward B. Lee, MD, PhD

None

Suzee E. Lee, MD

None

Iliya Lefterov, MD, PhD

None

Cynthia A Lemere, PhD

Cynthia Lemere serves as a paid consultant to AC Immune, Acumen Pharmaceuticals, ADvantage Therapeutics, Apellis Pharmaceuticals, Biogen, Cognition Therapeutics, Cyclo Therapeutics, Novo Nordisk, MEDAcorp, and Cambridge Healthcare Research Consulting Group. She serve as an unpaid advisor to the Alzheimer's Association, BrightFocus Foundation, Cure Alzheimer's Fund, LuMIND (DSMB), MODEL-AD and the US POINTER Study.

Allan I. Levey, MD, PhD

None

Stefan Lichtenthaler, PhD

None

Spencer W. Liebel, PhD

None

Lei Liu, MD, PhD

None

Peter A. Ljubenkov, MD

None

Justin M. Long, MD, PhD

I have no relevant financial disclosures. I served as sub-investigator for the Clarity AD study at the Washington University site.

Marissa Natelson Love, MD

I have served as a site investigator on the phase 2 trial for lecanemab and currently serve as the site Principal Investigator on a prevention trial involving lecanemab.

Val J. Lowe, MD

Dr. Lowe consults for Bayer Schering Pharma, Piramal Life Sciences, Life Molecular Imaging, Eisai Inc., AVID Radiopharmaceuticals, and Merck Research and receives support from GE Healthcare, Siemens Molecular Imaging, AVID Radiopharmaceuticals and the NIH (NIA, NCI).

Yvonne Lu, PhD, RN, FGSA, FAAN

None

Joseph C. Masdeu, MD, PhD

Investigator in the AHEAD Study

Gad A. Marshall, MD

Co-investigator on Clarity AD trial

Colin L. Masters

None

Eric McDade, DO

Institutional support (clinical trial): Eisai, Eli Lilly, Roche

Amy McLean, DNP

One advisory panel for Genentech

Scott M. McGinnis, MD

Site sub-investigator for CLARITY

Michael B. Miller, MD, PhD

None

David G. Morgan, PhD

Hesperos Inc, Bright Minds Biosciences

John C. Morris, MD

None

Richard G. M. Morris

None

Beth Mormino, PhD

NIH funding for research. Paid consultant to Eli Lilly, Neurotrack, and Hoffmann-La Roche.

Cath Mummery, MD, PhD

Consultant for Biogen, Eisai, IONIS, Roche, Lilly, Alnylam, Alector, WAVE but not directly involved with the lecanemab trials

Melissa E. Murray, PhD

Dr. Murray served as a paid consultant and receives grant

funding from Avid Radiopharmaceuticals.

Salvatore Napoli

None

Peter T. Nelson, MD, PhD

None

Aivi T. Nguyen, MD

None

Adrian L. Oblak, PhD

None

Kenjiro Ono, PhD, MD

None

Rik Ossenkoppele, PhD

None

Emily Paolillo, PhD

None

Mike Pappolla, MD, PhD

None

Victoria S. Pelak, MD

Site Investigator for Biogen EMBARK

Ronald Petersen, PhD, MD

Roche, Merck, Biogen, Eisai, Genentech, Lilly, Nestle, consultant; Genentech DSMB

Peter S. Pressman

None

Gil D. Rabinovici, MD, FAAN, FANA

Dr. Rabinovici receives research support (paid to institution) from Avid Radiopharmaceuticals, Life Molecular Imaging, GE Healthcare and Genentech. In the past 3 years he has served as a scientific advisor for Eli Lilly, GE Healthcare, Genentech,

Roche and Merck. He serves on a DSMB for Johnson & Johnson.

Rema Raman, PhD

Rema Raman has received funding from the National Institutes of Health, Alzheimer's Association, Eli Lilly for the A4 study (as a public-private partnership) and Eisai for the AHEAD 3-45 studies (as a public-private partnership). Dr. Raman was not involved in the CLARITY-AD trial. She is the Board Chair (unpaid) for the Alzheimer's Association's San Diego/Imperial chapter and a member of the Alzheimer's Association's AAIC Scientific Program Committee.

Vijay K Ramanan, MD, PhD

None

Kamalini Ranasinghe

None

Katherine P. Rankin, PhD

None

P. Hemachandra Reddy, PhD

None

R. Ross Reichard

None

Ashley Reiff LCSW

None

Dorene M. Rentz, PsyD

Dr. Rentz has served as a consultant of Biogen, Eisai and Novartis

Robert Rissman, PhD

None

Erik Roberson, MD, PhD

None

Julio C. Rojas, MD, PhD

Julio C. Rojas is a site PI for clinical trials sponsored by Eisai and Eli-Lilly.

Howard Rosen, MD

I have worked as a consultant for Genentech, Wave Neuroscience, Eisai, Otsuka, Takeda, Biogen, and Ionis pharmaceuticals

Owen A. Ross, PhD

None

Christopher C. Rowe, BMBS, MD, FRACP

Research grants to institution received from Biogen, Eisai, Actinogen, Cerveau technologies. Scientific Advisory Board payments received from Prothena, Roche, Eisai Australia, Lilly Australia

Marwan Noel Sabbagh MD, FAAN

None

Carl Sadowsky, MD

None

S Ahmad Sajjadi, MD, PhD

I have served on Eisai advisory committee for Lecanemab

Stephen Salloway, MD, MS

Dr. Salloway was the co-chair of the Investigator Steering Committee for the Aducanumab phase 3 program and he served as a site PI for the aducanumab and lecanemab phase 3 studies, the donanemab phase 2 trial and he was the Project Arm Leader for gantenerumab in DIAN-TU. He has provided consultation to Biogen, Lilly, Roche, Genentech, Bolden, Amylyx,

Prothena and Eisai. He has no stock or royalties related to any medication in development. Dr. Salloway serves on the planning committee for ALZ-NET and he is a member of the ADRD Therapeutics Work Group. He is the first author for the report of ARIA in aducanumab phase 3 (Salloway, JAMA Neurology, 2022), the report of gantenerumab and solanezumab in DIAN-TU (Salloway, Nature Medicine, 2021). He is a co-author on the report of the donanemab phase 2 trial (Mintun, NEJM, 2021) and the Aducanumab Appropriate Use Recommendations (Cummings, Journal of the Prevention of Alzheimer's Disease, 2021, 2022).

Rowan Saloner, PhD

None

Kumar Sambamurti, PhD

None

Andrew J. Saykin, PsyD

Dr. Saykin has received support from Avid Radiopharmaceuticals, a subsidiary of Eli Lilly (in kind contribution of PET tracer precursor); and consulted for Bayer Oncology (Scientific Advisory Board); Eisai (Scientific Advisory Board); Siemens Medical Solutions USA, Inc. (Dementia Advisory Board); NIH NHLBI (MESA Observational Study Monitoring Board); and Springer-Nature Publishing (Editorial Office Support as Editor-in-Chief, Brain Imaging and Behavior).

Prof. Philip Scheltens, MD, PhD

None

Julie Schneider

Consultant, Lilly and AVID Radiopharmaceuticals, Cerveau Technologies, Inc., National Hockey League, Takeda Development Centers Americas, Inc.

Michael Schöll, PhD

MS has research agreements with Roche and has consulted with Servier, NovoNordisk and Roche.

Professor Jonathan M. Schott, MD FRCP FAAN

I have received research funding and PET tracer from AVID Radiopharmaceuticals (a wholly owned subsidiary of Eli Lilly) and Alliance Medical; have consulted for Roche, Eli Lilly, Biogen, Merck and GE; received royalties from Oxford University Press, and Henry Stewart Talks. I am Chief Medical Officer for Alzheimer's Research UK, and Clinical Advisor to UK Dementia Research Institute.

Julie Schwartzbard

None

Dennis Selkoe, MD

Director and consultant to Prothena Biosciences. Ad hoc consultant to Eisai

Sharon J. Sha, MD, MS

None

Leslie M. Shaw, PhD

None

Eric Siemers, MD

Chief Medical Officer, Acumen Pharmaceuticals; Consultant, Vaccinex Inc.

Bryan Luke Smesler

None

Amanda G. Smith, MD

Our site is a study site for CLARITY AD and we receive research grants from Eisai.

B. Joy Snider, MD, PhD

Site Principal investigator for Eisai sponsored Clarity trial

Peter J. Snyder, PhD

None

Deborah Sokol, PhD, MD, ABCN

None

Weihong Song

None

Michelle Sorweid, DO, MPH

None

Reisa Sperling, MD

Dr. Sperling co-leads the AHEAD Study which is testing lecanemab at an earlier stage of preclinical Alzheimer's disease, and receives research support from Eisai and the NIH for this public-private partnership clinical trial.

Salvatore Spina, MD, PhD

Dr. Spina has received consultations honoraria from Techspert.io, Acel Health, Precision Xtract, and Putnam.

Adam M. Staffaroni, PhD

Paid consultant to Alector, Eli Lilly/Prevail, Passage Bio, and Takeda

Susan Steen, MD
None

Andrew Stern, MD, PhD
None

David Tanne
None

Carmela Tartaglia
I run clinical trials in AD medications: Biogen, Janssen, Avanex, Roche, Green Valley, Merck, UCB, Novo Nordisk, Passage Bio.

Malu G. Tansey, PhD
MGT is a member of the Medical and Scientific Advisory Group (MSAG) of the Alzheimer's Association

Boon Lead Tee, MD
None

Marilù Gorno Tempini, MD, PhD
None

David B. Teplow, PhD
None

Mahendra Kumar Thakur
None

Paul M. Thompson, PhD
PMT received research grant funding from Biogen, Inc., for research unrelated to this topic.

Lars Olof Tjenberg, PhD
None

Taisuke Tomita, PhD
None

Elena Tsoy, PhD
None

Raymond Scott Turner
Research support to Georgetown University from Lilly, Eisai, Biogen, and Roche/Genentech.

Lawren VandeVrede, MD, PhD
None

Robert Vassar, PhD
I have been an ad hoc consultant for Eisai's BACE inhibitor program.

Prashanthi Vemuri, PhD
Funded by the NIH.

Everard (Jort) Vijverberg, PhD, MD
PI of clinical trials from AC immune, CogRX therapeutics, New Amsterdam Pharma, Janssen, UCB, Roche, GreenValley, Vivoryon, ImmunoBrain, GemVax, Alzheon, DIAN-TU and Alector, and sub-I from trials from Eli Lilly, Cortexyme, Biogen en Fujifilm Toyama.

Consultant for New Amsterdam Pharma, Treeway, ReMynd, Vivoryon, Biogen, Vigil Neuroscience and ImmunoBrain Checkpoint.

Qing Wang, PhD
None

Ruizhi Wang
None

David Weisman
I was site PI on the phase 2b trial of lecanemab. Currently site PI on AHEAD study with lecanemab.

Meredith Wicklund, MD
None

Michael W. Weiner, MD
Dr. Weiner serves on Editorial Boards for Alzheimer's & Dementia, and the Journal for Prevention of Alzheimer's disease. He has served on Advisory Boards for Acumen Pharmaceutical, Alzheon, Inc., Cerecin, Dolby Family Ventures, Merck Sharp & Dohme Corp. and NervGen. He also serves on the USC ACTC grant which receives funding from Eisai for the AHEAD study.

He has provided consulting to Baird Equity Capital, BioClinica, Cerecin, Inc., Cytox, Dolby Family Ventures, Duke University, Eisai, FUJIFILM-Toyama Chemical (Japan), Garfield Weston, Genentech, Guidepoint Global, Indiana University, Japanese Organization for Medical Device Development, Inc. (JOMDD), Medscape, Nestle/Nestec, NIH, Peerview Internal Medicine, Roche, T3D Therapeutics, University of Southern California (USC), WebMD, and Vida Ventures.

He has acted as a speaker/lecturer to The Buck Institute for Research on Aging; China Association for Alzheimer's Disease (CAAD); Japan Society for Dementia Research; and Korean Dementia Society, and the following entities have provided funding for academic travel; University of Southern California (USC), NervGen, ASFNR, and the AD/PD and CTAD Congresses.

He holds stock options with Alzheon, Inc., Alzeca, and Anven.

Dr. Weiner received support for his research from the following funding sources:

National Institutes of Health (NIH), Department of Defense (DOD), Patient-Centered Outcomes Research Institute (PCORI), California Department of Public Health (CDPH), University of Michigan, Siemens, Biogen, Hillblom Foundation, Alzheimer's Association, The State of California, Johnson & Johnson, Kevin and Connie Shanahan, GE, VUmc, Australian Catholic University (HBI-BHR), The Stroke Foundation, and the Veterans Administration.

Alexander White, MD

I am conducting BAN2401 301.

Donna M Wilcock, PhD

None

Charles Windon, MD

Funding from NIH, Alzheimer's Association, LCN consulting

David A. Wolk, MD

I have received consulting fees from Eli Lilly, Qynapse, and GE Healthcare. I am site-PI of a study with Biogen (EMBARK) and have served on the DSMB for Functional Modulation.

Benjamin Wolozin, MD, PhD

I declare a conflict of interest because I am CSO and Co-Founder of Aquinnah Pharmaceuticals Inc.

Bryan Woodruff, MD

I have participated in industry-sponsored trials of investigational treatments for Alzheimer's disease, but not specifically studies of lecanemab.

Pauline Wu, DO

None

Heather Wynne-Phillips, MSN, APRN, FNP-C

Our institution is a study site for CLARITY AD and we receive research grants from Eisai.

Hyun-Sik Yang, MD

None

Keir Yong, PhD

None

Tracy Young-Pearse

None

Ehud Zeltzer, MD

None

Henrik Zetterberg, MD, PhD

HZ has served on scientific advisory boards and/or as a consultant for Abbvie, Acumen, Alector, ALZPath, Annexon, Apellis, Artery Therapeutics, AZTherapies, CogRx, Denali, Eisai, Nervgen, Novo Nordisk, Passage Bio, Pinteon Therapeutics, Red Abbey Labs, reMYND, Roche, Samumed, Siemens Healthineers, Triplet Therapeutics, and Wave, has given lectures in symposia sponsored by Cellectricon, Fujirebio, Alzecure, Biogen, and Roche, and is a co-founder of Brain Biomarker Solutions in Gothenburg AB (BBS), which is a part of the GU Ventures Incubator Program.

Serggio Lanata, MD, MS

None

Takeshi Iwatsubo, MD

Scientific Advisor for Eisai, Biogen and Eli Lilly