NAPA Research Subcommittee
Overview of Scientific Advances, Opportunities, and Challenges

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Dr. Randall J. Bateman – Disclosure

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DIAN-TU Pharma Consortium: Active: Biogen, Eisai, Eli Lilly & Co., Janssen, Roche/Genentech. *Previous: AbbVie, Amgen, AstraZeneca, Forum, Mithridion, Novartis, Pfizer, Sanofi, United Neuroscience*
DIAN-TU Trial Companies: Eli Lilly and Co., Roche, Janssen, Eisai, Avid Radiopharmaceuticals, Cerveau Technologies

Invited Speaker (12 months):
Editorial Board: Alzheimer's and Dementia, Alzheimer's Research and Therapy, The Journal of Prevention of Alzheimer's Disease
Consulting Relationships (12 months): Roche – GSMs for Autosomal Dominant AD Committee (unpaid)

Companies:

- Dr. Randall J. Bateman co-founded C2N Diagnostics and receives income from C2N Diagnostics for serving on the scientific advisory board. Washington University has equity ownership interest in C2N Diagnostics.
  - Dr. Bateman is an inventor of the stable isotope labeling kinetics, blood plasma assay, methods of diagnosing AD with phosphorylation changes, neurofilament light chain assays and materials, and newer tau assays technologies licensed by Washington University to C2N Diagnostics. Through these relationships, Washington University, Dr. Bateman is entitled to receive royalties and/or equity from the license agreement with C2N.
  - C2N Diagnostics will be analyzing samples from the Knight Family DIAN-TU-001 trial of E2814 for primary, secondary, and exploratory endpoints. Should the DIAN-TU trials impact the value of C2N Diagnostics, Washington University (WU) and Dr. Randall Bateman could directly benefit.

NAPA goal to prevent and effectively treat AD/ADRD by 2025 – progress and current landscape

- FDA traditional approval of lecanemab (Leqembi) July 2023
- CMS coverage for lecanemab with physician participation in CMS-facilitated registry
- Positive results from Phase 3 study of donanemab (July 2023), FDA traditional approval decision pending
- Blood-based biomarkers (amyloid-β 42/40, p-tau217, and others) identify amyloid pathology with high accuracy and are on market for clinical use, but not yet FDA or payer approved, or used routinely in practice
- Aggressive blood pressure lowering in persons with vascular risk factors reduced the combined outcome of cognitive impairment/dementia

Groundbreaking advancements in AD/ADRD research were made possible by increases in federal funding

- $226 million increase in Congress' appropriations in FY23
- Annual federal funding for Alzheimer's and related dementias research is now approximately $3.7 billion
- The NIH is currently funding 488 active clinical trials for AD and ADRD prevention, treatment, and caregiving, including over 170 non-pharmacological interventions

What still needs to be done?

- Research to answer outstanding questions on current disease-modifying therapies for AD
- Development and testing of additional drug candidates in more representative, efficient, and practical clinical trials
- Better biomarkers and treatments for ADRD
- Increase knowledge of risk and protective factors in individuals and across diverse populations
- Pursue a precision medicine approach to detect the disease earlier and tailor treatment plans to an individual's unique disease and risk profiles
- Leverage emerging digital technologies and big data to speed discoveries

Congress must continue its commitment to the fight against Alzheimer's by increasing research funding in FY24

- As of January 17, 2024, NIH remains under a continuing resolution (CR) through February 2, 2024:

	NIA Funding Line Policy for FY 2023	NIA Interim Funding Line Policy for FY 2024	
	AD/ADRD payline	**AD/ADRD payline, <$5M**	**AD/ADRD payline, ≥$5M**
All (except below)	25%	12%	10%
New investigator R01s	28%	15%	13%
Early stage investigator R01s	30%	17%	15%

Strong, sustainable, and predictable funding is critical for AD/ADRD research

- The CR has led to implementation of conservative interim paylines, profoundly impacting the percentage of new research projects that can be funded.
  - For example, 1 in 4 AD/ADRD projects with budgets of >$5M were funded in FY 2023 compared to 1 in 10 during FY 2024.
  - Many researchers who submitted grants that were in the fundable range in FY23 needed to revise and resubmit their applications, leading to countless additional hours spent preparing applications (time that could have been spent conducting research) and significant delays in research funding.
- There is an urgent need for Congress to increase annual federal research funding to meet NAPA goals.
  - Rising costs of research year over year is a major concern – even a flat budget with no cuts means declined buying power and less research can be done.