

# Research Progress on Alzheimer's Disease and Related Dementias

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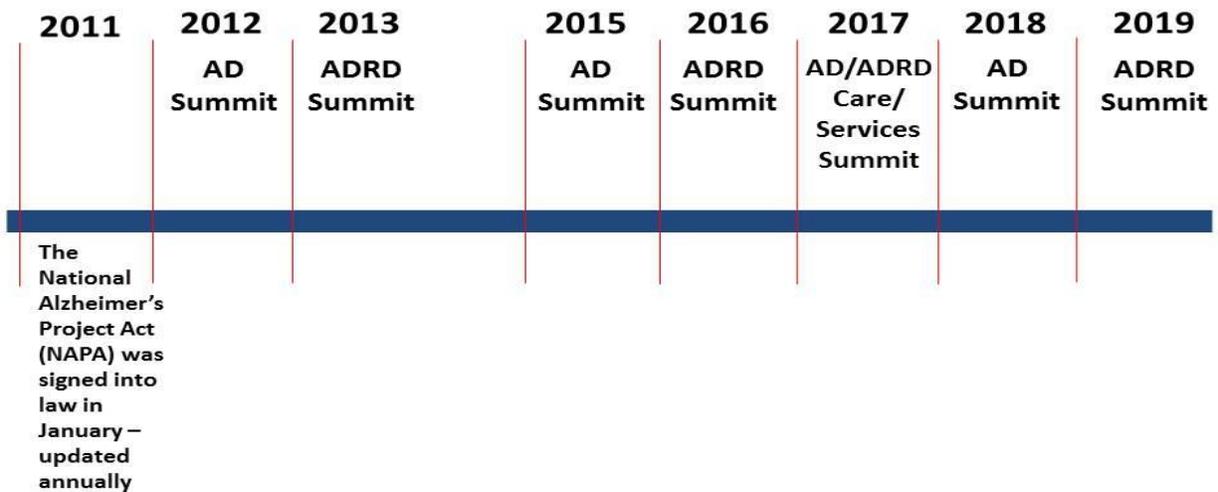
## NAPA Advisory Council Meeting

Richard J. Hodes, M.D.  
Director  
National Institute on Aging

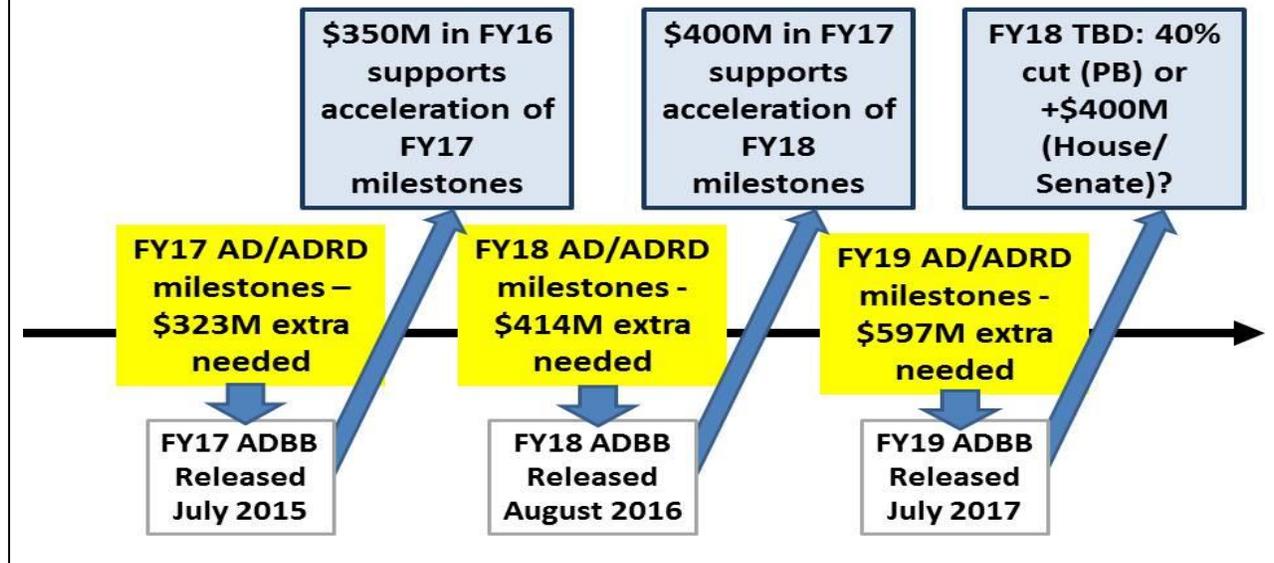
January 26, 2018

# Research Implementation Milestones: Our Central Driver

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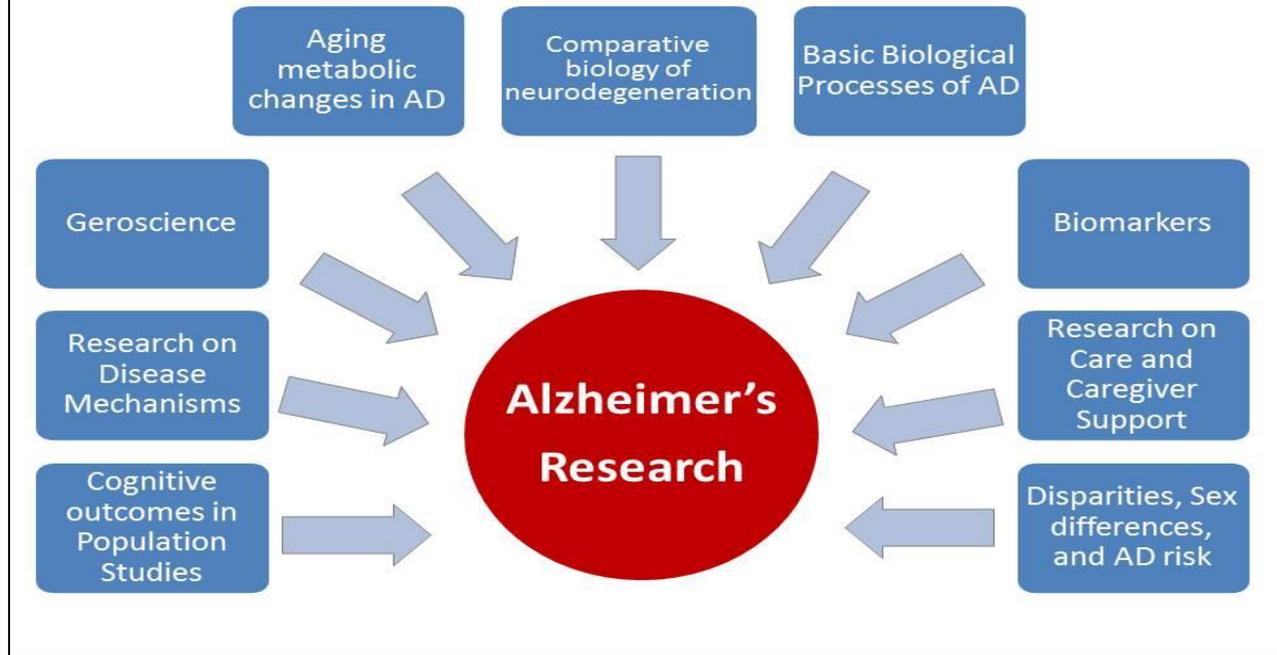
## Recent Investments Allow Us to Accelerate Milestones - ADBB Timing and Appropriations



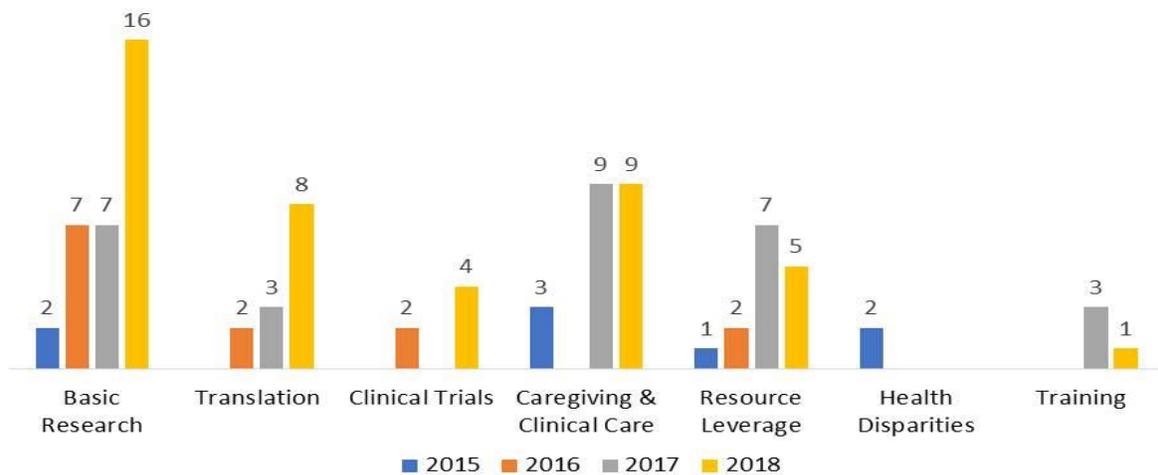
## What Counts as AD/ABDR Research?

- The AD/ABDR pay line applies to applications/awards that are coded as AD or Alzheimer's disease - related dementias (ABDR)
- The ABDR RCDC categories that report related dementias specifically named in the National Plan to Address Alzheimer's Disease are:
  - Lewy Body dementia (LBD)
  - Frontotemporal dementia (FTD)
  - Vascular Cognitive Impairment/Dementia (VCI/D)

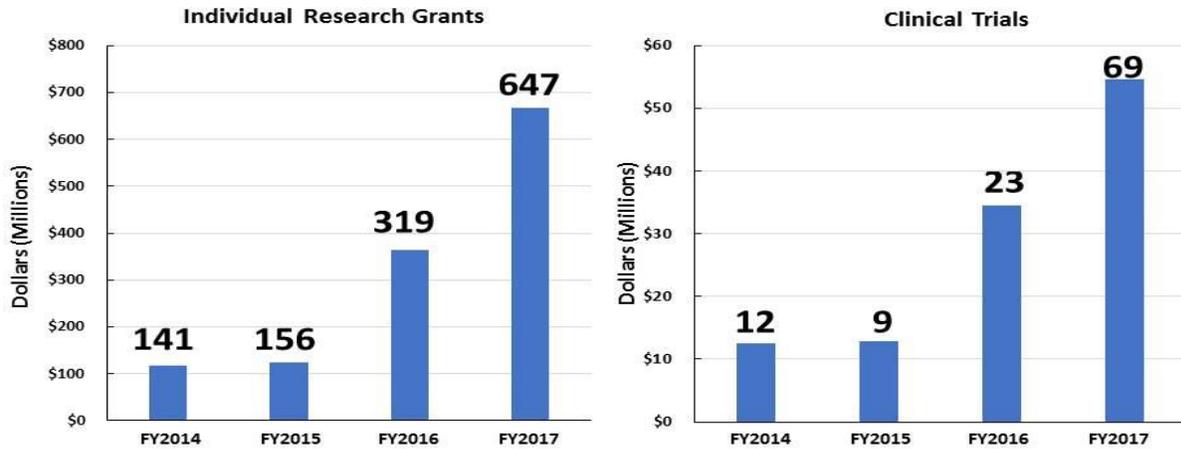
## Diversity of AD/ADRD Research



## AD/ADRD FOAs by Fiscal Year

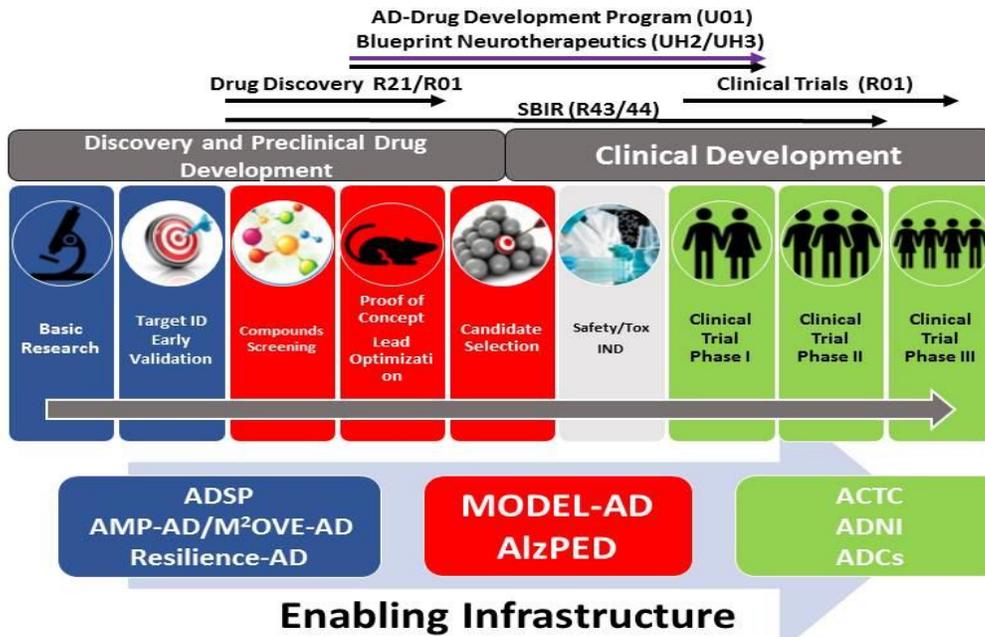


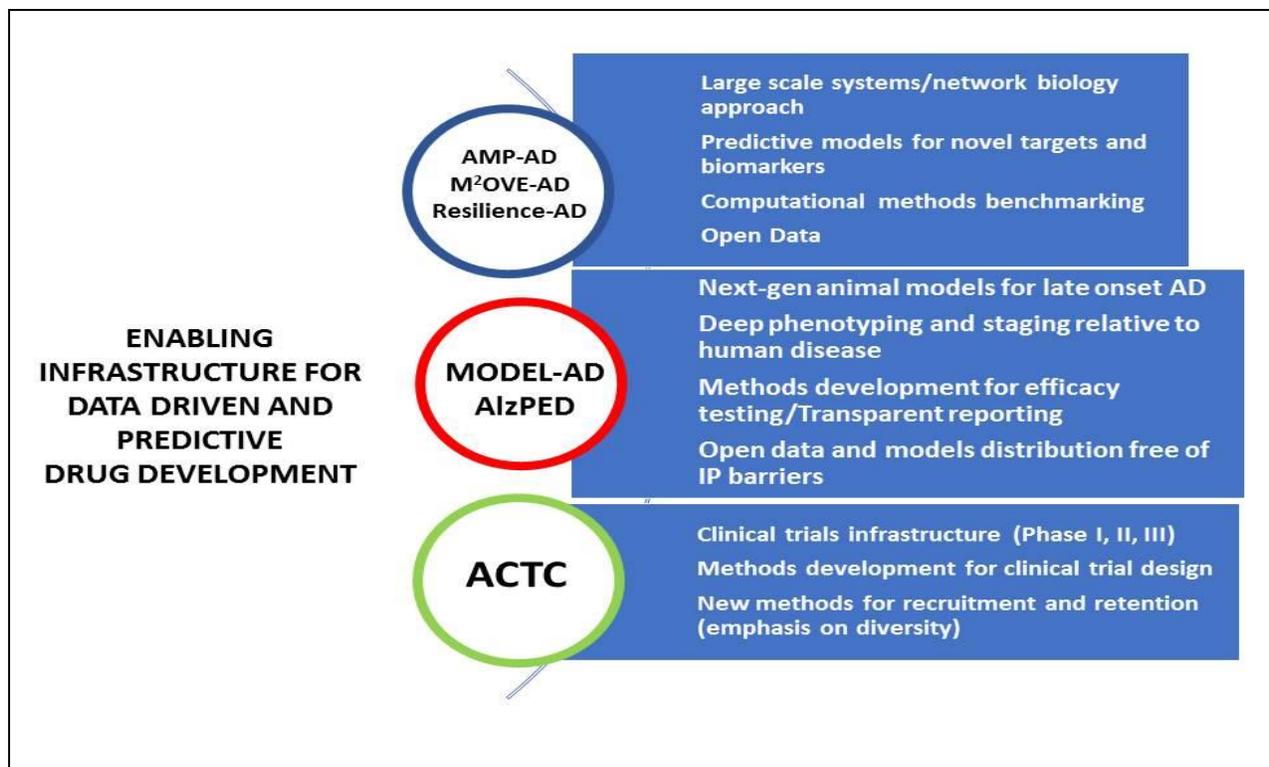
## AD and ADRD Research Investments FY14-FY17



These figures show grants awarded with NIA funding. Some of the grants are in response to initiatives sponsored by NIH ICs other than NIA (e.g., NINDS, NIBIB, NIEHS, NIDCD).

## Translational Programs and Infrastructure for AD and ADRD





## Ongoing NIA AD/ADRD and Related Intervention and Prevention Trials

- Over 140 active trials
- 40 Early-stage Clinical Drug Development (Phase I and Phase II Clinical Trials)
  - Amyloid (9)
  - Neurotransmitter Receptors (3)
  - Metabolism and Bioenergetics (4)
  - Vasculature (3)
  - Growth Factors and Hormones (1)
  - Multi-target (6)
  - Oxidative Stress (1)
- 8 Late-stage Clinical Drug Development (Phase II/III and Phase III Clinical Trials)
  - Amyloid (6)
  - Vasculature (2)
- 62 Non-Pharmacological Interventions
  - Exercise (16)
  - Diet (2)
  - Cognitive Training (20)
  - Combination Therapy (11)
- 7 Clinical Therapy Development for the Neuropsychiatric Symptoms of AD/ADRD
  - Pharmacological (5)
  - Non-Pharmacological (2)
- 37 Care and Caregiver Interventions

## Specific Milestone-Directed Achievements

**Milestone 6.D:** Identify, characterize, and complete early validation for at least six novel therapeutic targets for AD (a minimum of three targets for presymptomatic and early-stage disease and a minimum of three for advanced disease). These efforts should include therapeutic targets for the neuropsychiatric and behavioral disturbances in AD. Validation based on availability of the following for each novel target: a systems-level understanding of the gene, protein, and metabolic networks within which they operate, one or more cell-based/animal models that are freely available to the research community, a quantitative assessment of the integrative response to the modulation of the target in one or more model organisms, and identification of pharmacodynamic biomarker(s) for target engagement. [2012 AD Summit: 1A, 1B, 1D, and 5A]

2012	2013	2014	2015	2018
<a href="#">RFA AG 13-013</a> Interdisciplinary Approach to Identification and Validation of Novel Therapeutic Targets for Alzheimer's Disease (R01)	4 R01 projects funded and converted into U01 mechanism	2 additional R01s funded and incorporated into AMP-AD Target Discovery and Preclinical Validation Project/ Consortium	<a href="#">AMP-AD Knowledge Portal</a> launched as a platform for sharing multi-omics data and analytical results/network models	Data generation completed, data and network models made available to researchers at large

## Specific Milestone-Directed Achievements

**Milestone 6.F:** Initiate first in human Phase I drug trials for therapeutic agents against at least six novel therapeutic targets. In addition to safety, these trials will provide evidence of target engagement. [2012 AD Summit: 3A, 3B, 3F, and 5E]

**Milestone 6.G:** Initiate Phase II (proof-of-concept) drug trials for agents against three to six novel therapeutic targets. These trials will provide proof of mechanism and/or evidence of target engagement of the target being tested. [2012 AD Summit: 3A, 3B, 3F, and 5E]

2012	2014	2015	2016
<a href="#">RFAAG 13-016</a> Alzheimer's Disease Phase I Clinical Trials (R01)	Funded a Phase I Trial to test the safety of Allopregnanolone as a novel neuroregenerative therapeutic for AD	<a href="#">PAR 16-365</a> Pilot Clinical Trials for the Spectrum of Alzheimer's Disease and Age-related Cognitive Decline (R01)  Funded a Phase I Trial to test the safety of a first in class PDE4 allosteric modulator as a novel therapeutic for MCI	Funded a Phase II Trial to test the efficacy of a first in class P75NTR ligand as a novel neuroprotective AD therapeutic



**LM11A-31** - first in class, small molecule modulator of the P75 Neurotrophin Receptor

*PI – Frank Longo MD and NeurotrophiX*

The pre-clinical drug development and part of the IND-enabling studies for **LM11A-31** were supported through NIA's AD Translational Research Program

The Phase II trial is being supported through NIA's Pilot Clinical Trials Program via [PAR 16-365](#)

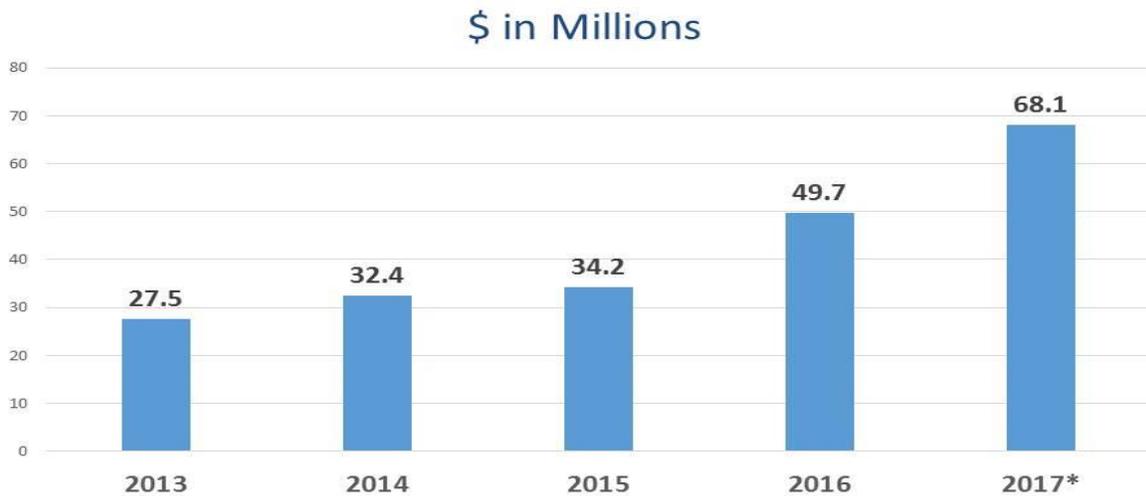
## Opportunities for Small Business – AD/ADRD specific

- **Advancing Research on Alzheimer's Disease (AD) and Alzheimer's-Disease-Related Dementias (ADRD) (R41/R42/R43/R44)**
- **Tools for Clinical Care and Management of Alzheimer's Disease (AD) and its Comorbidities (R41/R42/R43/R44)**
- **Development of Socially-Assistive Robots (SARs) to Engage Persons with Alzheimer's Disease (AD) and AD-Related Dementias (ADRD), and their Caregivers (R41/R42/R43/R44)**

<https://www.nia.nih.gov/research/grants-funding/small-business-innovation-research-and-technology-transfer-programs>

## NIA SBIR/STTR Obligations

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\* Estimate

## NIH AD Research Summit - March 1-2, 2018: Path to Treatment and Prevention

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The program agenda is organized around seven sessions:

- Novel Mechanistic Insights into the Complex Biology and Heterogeneity of AD
- Enabling Precision Medicine for AD
- Translational Tools and Infrastructure to Enable Predictive Drug Development
- Emerging Therapeutics
- Understanding the Impact of the Environment to Advance Disease Prevention
- Advances in Disease Monitoring, Assessment and Care
- Building an Open Science Research Ecosystem to Accelerate AD Therapy Development

<https://www.nia.nih.gov/research/nih-ad-summit-2018-program-agenda#agenda>

## FY2018 NINDS ADRD Funding Opportunity Announcements

### [PAR-18-413](#) Mechanistic Basis of Diffuse White Matter Disease and Small Vessel Pathology in Vascular Contributions to Cognitive Impairment and Dementia (VCID)(R01)

- To support hypothesis-testing research to elucidate cellular and molecular mechanisms that underlie diffuse white matter disease and small vessel disease in the brain, the relationships between them, and their contributions to cognitive impairment and dementia
- **Application are due [March 23, 2018](#)**

### [RFA-NS-18-017](#) Planning Grant to Develop Phase III Clinical Trials for Lewy Body Dementia (R34)

- To provide one year of support for planning activities necessary for initiating a Phase III clinical trial designed to treat patients with LBD
- **Applications are due [March 20, 2018](#)**

### **NINDS is planning to release 4 additional new ADRD FOAs for FY18**

- See the approved research concepts in the NINDS [Director's Message](#) on the NINDS website!

***Save the date!* ADRD Summit (III)**  
**March 14-15, 2019**

Location: Natcher on the NIH Main Campus, Bethesda MD

## January 26, 2018 -- Advisory Council Meeting #27

The meeting was held on Friday, January 26, 2018, in Washington, DC. The Research Subcommittee took charge of this meeting's theme, focusing on the process from targets to treatments. The Council heard speakers on the preclinical pipeline, the clinical trial pipeline, and the industry perspective. The meeting also included discussion of a driver diagram to guide the Council's future work, updates and a report from the October Care Summit, and federal workgroup updates. Material available from this meeting is listed below and is also available at <https://aspe.hhs.gov/advisory-council-alzheimers-research-care-and-services-meetings#Jan2018>.

Comments and questions, or alerts to broken links, should be sent to [napa@hhs.gov](mailto:napa@hhs.gov).

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### General Information

<b>Agenda</b>	<a href="#">[HTML Version]</a> <a href="#">[PDF Version]</a>
<b>Meeting Announcement</b>	<a href="#">[HTML Version]</a> <a href="#">[PDF Version]</a>
<b>Meeting Summary</b>	<a href="#">[HTML Version]</a> <a href="#">[PDF Version]</a>
<b>Public Comments</b>	<a href="#">[HTML Version]</a>

### Handouts

<b>Care Summit Report Themes</b>	<a href="#">[PDF Version]</a>
<b>NAPA Driver Diagram Draft Examples</b>	<a href="#">[PDF Version]</a>
<b>Outline for Care Summit Final Report</b>	<a href="#">[PDF Version]</a>

### Presentation Slides

<b>AbbVie's R&amp;D Vision for Alzheimer's Disease</b>	<a href="#">[HTML Version]</a> <a href="#">[PDF Version]</a>
<b>Care Summit Report</b>	<a href="#">[HTML Version]</a> <a href="#">[PDF Version]</a>
<b>Clinical Subcommittee Update</b>	<a href="#">[HTML Version]</a> <a href="#">[PDF Version]</a>
<b>Initiatives, Partnerships and Collaboration to Help Patients with the Highest Unmet Need: Dominantly Inherited Alzheimer's Disease Trials Unit (DIAN-TU) as a Case Example</b>	<a href="#">[HTML Version]</a> <a href="#">[PDF Version]</a>
<b>Long-Term Services and Supports Committee Update</b>	<a href="#">[HTML Version]</a> <a href="#">[PDF Version]</a>

<b>NAPA Driver Diagram</b>	<a href="#">[HTML Version]</a> <a href="#">[PDF Version]</a>
<b>Overview of the Clinical Trial Pipeline for AD</b>	<a href="#">[HTML Version]</a> <a href="#">[PDF Version]</a>
<b>Overview on NIA Preclinical Pipeline</b>	<a href="#">[HTML Version]</a> <a href="#">[PDF Version]</a>
<b>Participating in an Alzheimer's Clinical Study: Perspectives on Involvement of a Person Living with Dementia and Her Study Partner</b>	<a href="#">[HTML Version]</a> <a href="#">[PDF Version]</a>
<b>Progress Since October</b>	<a href="#">[HTML Version]</a> <a href="#">[PDF Version]</a>
<b>Research Progress on Alzheimer's Disease and Related Dementias</b>	<a href="#">[HTML Version]</a> <a href="#">[PDF Version]</a>
<b>Research Subcommittee Agenda: The Journey from Targets to Treatments</b>	<a href="#">[HTML Version]</a> <a href="#">[PDF Version]</a>

## **Videos**

<b>Updates since October meeting</b>	<a href="#">[Video]</a>
<b>NAPA Driver Diagram</b>	<a href="#">[Video]</a>
<b>Federal Updates</b>	<a href="#">[Video]</a>
<b>Public Comments</b>	<a href="#">[Video]</a>
<b>Research Subcommittee Agenda</b>	<a href="#">[Video]</a>
<b>Care Summit Update</b>	<a href="#">[Video]</a>

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Last Updated: 06/09/2018