

Research Subcommittee Draft Recommendations and Feedback on Draft National Plan

March 14, 2012

This preliminary document represents initial ideas of the Research Subcommittee, but there are multiple additional issues that we will discuss between now and April.

Overall Goal

To substantially delay the onset or slow the progression of Alzheimer's Disease by 2020, and to prevent and effectively treat Alzheimer's Disease by 2025.

Setting the goal of preventing and effectively treating Alzheimer's by 2025 is bold yet achievable with adequate resources and an outcomes-oriented, milestones-driven plan. This goal also sets interim milestones to track successful progress toward the achieving the 2025 goal by calling for the availability to the public of significant disease-modifying or substantially-enhanced symptom-mitigating behavioral or pharmacologic interventions by 2020.

While these goals of making new remedies for AD available by 2020 and 2025 are ambitious, they should not be interpreted as favoring translational drug development over basic discovery. Scientists do not yet fully understand the cellular, inflammatory and tissue mechanisms that lead to Alzheimer's disease, and our ability to identify environmental influences (and thus potentially modifiable risk factors) on disease progression is also as yet incomplete. Therefore, new investment in basic research and drug discovery must reflect a critical balance between long-term investment and the urgency of immediate progress to our nation's fiscal and public health.

Underlying these goals is the high priority for development of a clear plan and roadmap of specific research and drug discovery priorities and milestones for achieving the goal of preventing and effectively treating Alzheimer's by 2025 and its interim 2020 targets. This roadmap must comprehensively span the entire scope of work that must occur, and should identify and marshal not only existing resources within the Federal government, but also new resources from within and without the Federal government, including new private-public partnerships, incentives for increased private investment, and mobilization of global investments.

The credibility of a 2020 interim goal is supported by increasing evidence of lifestyle or behavioral interventions that may delay the onset of Alzheimer's disease or slow progression of cognitive decline. These interventions may have a significant role in reducing the societal burden of Alzheimer's even if the underlying mechanism of their effectiveness is as yet unknown. The current and planned scope of this research should be assessed and prioritized within the more comprehensive research roadmap referred to above.

The subcommittee's recommended strategies, in part, for achieving this goal are to:

- Commit resources with accountability
- Accelerate development of effective treatments
- Maximize private investment to develop treatments
- Meaningfully coordinate with global partners

Potential action items for these strategies are discussed below.

Commit Resources with Accountability

Commit aggressive resources, with appropriate accountability, to Alzheimer's disease research to match the current and growing impact of the disease on society.

1. In order to reach the 2025 goal, there is an urgent need for annual federal research funding to be ramped up to a minimum of \$2 billion in targeted, outcome-oriented Alzheimer's research initiatives spanning basic, translational and clinical research. Recipients of this funding would be accountable for progress toward the overall stated goal. (non-Federal members are discussing this)

Potential Action Steps:

- The Administration and Congress should propose and support a rapid ramp up to \$2 billion in Alzheimer's research at NIH.
 - In conjunction with the strategic research plan (Action 1B) in the Draft National Alzheimer's Plan, NIH will develop budget estimates that will outline future investments in federal Alzheimer's research and build those investments into their annual budget requests.
 - NIH will coordinate with other federal agencies to ensure their federal Alzheimer's funding complements the NIH's investments and enhances progress towards the goal of preventing and effectively treating Alzheimer's by 2025.
2. HHS should be required to develop, execute and regularly update a scientific research plan and priorities to accelerate breakthroughs in AD research, a review of research infrastructure including public/private partnerships, and provide programmatic recommendations for achieving these targeted research opportunities through sustainable higher levels of annual funding.

Potential Action Steps:

- The Director of NIH should lead a rigorous scientifically based strategic planning process for the conduct, coordination, and support of the

Alzheimer's research portfolio across all Institutes and Centers of the NIH. The research plan could:

- Identify emerging scientific opportunities, knowledge gaps, and priority research to be conducted by NIH and provide recommendations for achieving these targeted research opportunities with specified milestones;
 - Identify opportunities to incorporate Alzheimer's disease research in all relevant aging; neuroscience; basic, clinical, and translational science; trans-NIH; innovative; and non-traditional initiatives (this should include the Cures Acceleration Network and the National Center for Advancing Translational Sciences);
 - Review and improve existing Alzheimer's programs and initiatives at NIH, including consolidation or expansion of program activities, if such consolidation or expansion would improve program efficiencies and research outcomes;
 - Identify gaps in the supporting infrastructure and the coordination of the Alzheimer's research portfolio across the Institutes and Centers of the NIH, including the Alzheimer's Disease Centers Program and all intramural and extramural Alzheimer's-related activities;
 - Identify public-private partnership opportunities;
 - Identify opportunities to increase research and improve outcomes for women and minority populations at high-risk of developing Alzheimer's.
3. A person or office should be identified who has responsibility and accountability for execution of, and advocacy for, all aspects of the National Plan, including responsibility for issuing reports to Congress and the Advisory Council.
- This office should be positioned within the Executive Branch such that the work of multiple agencies can be monitored and directed
 - By the end of 2012, this office should identify a system of metrics for assessing annual progress toward the goals, develop a reporting dashboard for use by HHS, the Advisory Council and Congress and recommend mid-course corrections where annual measures of progress are not met.

Accelerate Development of Effective Treatments

Accelerate public access to new therapeutic interventions by compressing the current average time in the process of identification of therapeutic targets, validation of those targets, development of behavioral and pharmacologic interventions, testing of efficacy and safety, and regulatory review.

1. Develop behavioral and biological markers for potential therapeutic targets or surrogate endpoints.

Potential Action Steps:

- Identify genetic, family history, medical comorbidities, biomarkers, and clinical features in asymptomatic persons that are risk or protective factors for AD path physiology and ultimately AD clinical symptoms. Consider the establishment of large, representative cohorts of subjects at risk for the disease on which to develop and test the prediction models.
 - Catalogue existing Alzheimer's biological and behavioral marker initiatives including their current development and review, and identify gaps and a plan for addressing them. Update this plan annually.
 - Develop a focused action plan aimed specifically at identifying and validating early behavioral and biological markers for Alzheimer's disease using already established cohorts. This will be a subset of the larger research prioritization and action plan.
 - Issuance, upon endpoint approval, of unambiguous guidance on the use of behavioral and biological markers to industry on their usage.
2. The HHS Secretary, in consultation with the private sector, the research community and NGO's, should, by year-end 2012, model and prioritize the action steps needed to reduce the time for moving therapies from target identification and validation through regulatory approval and thereafter to implement or cause to be implemented such action steps.
 3. Develop a process by which research priorities aimed at accelerating the delivery of effective treatments would be set, including input from scientific experts.

Potential Action Steps:

- Establish research priorities agreed upon by NIH, FDA, and industry and establish a clear plan -- including specific milestones -- to advance each priority. The first specific plan of research priorities and action steps should be developed out of the May 2012 Alzheimer's Research Summit.
- Establish a joint NIH/NIA and Industry Alzheimer's working group which will and serve as an opportunity to foster government and industry collaboration and to inform the research priorities.
- Develop, in consultation with industry, a strategy for the increased standardization, disclosure, pooling and analysis of clinical trial data for current, future and past trials, biomarker data, and pre-clinical mouse models.
- Support, with the cooperation and participation of industry, researchers and NGO's, one or more open-architected registries of potential clinical trial participants designed to reduce the time and cost of clinical trial recruitment and to enhance the participation of women and minorities.

4. To address disparities, activities aimed at translation of research findings into medical practice and to the public should include specific targets for outreach to racial/ethnic, socioeconomic and younger populations who have been shown to be at the greatest risk for developing AD.
5. Develop metrics for assessing the effectiveness of therapies on the healthcare economy.

Maximizing Private Investment to Develop Treatments and Improve Disease Monitoring Technology

Explore policies that would encourage private industry to invest aggressively in disease-modifying interventions, to invest in technologies that improve our ability to detect the disease as early as possible, and monitor the disease accurately so that the effectiveness of interventions can be tested.

Potential Action Steps:

- Survey industry players at all levels (pharma, biotech, medical device, test publishers) engaged in Alzheimer's disease-related work to determine what government resources and policies would help to maintain or increase their commitment to Alzheimer's research.
- As part of the larger NAPA agenda, establish a process or mechanism for securing sustained industry input on topics such as measures to spur discovery and streamline regulatory review, tax, Intellectual Property, and other incentives.
- Dedicate a portion of Alzheimer's research funding each year to advanced research, SBIR, STTR and related initiatives to promote advanced research and support small businesses engaged in this work.
- Advance the other related actions include under other strategies (e.g., the industry engagement with NIH, research prioritization, behavioral and biomarker and endpoint validation, etc.) that are already known to be of importance to the industry.

Meaningful Coordination with Global Partners

Expand and enhance coordination with global partners and move forward to establish of a Global Alzheimer's Plan to respond to the global scope of the problem.

Potential Action Steps:

- Convene a meeting of all nations or regions with National/Regional Alzheimer's Plans in place or under development by 2013 to share best practices, learn lessons and foster global coordination.
- Identify a single high-level U.S. official as the point person for the National Alzheimer's Plan and appoint that person to represent the nation as part of an ongoing dialogue with global counterparts.

- Establish a framework for building upon initiatives like ADNI to foster greater global collaboration and coordination.
- Issue a call for action by nations who currently have or who are developing National Alzheimer's Plans. This call will urge specific measurable actions and a summit dedicated specifically to combating Alzheimer's (this has synergies with Peter Piot's call for action at the ADI conference).
- Foster ongoing international dialogue on Alzheimer's regulatory review and related issues.