Research Subcommittee Recommendations

January 14, 2014

1. **In order to support the goal to prevent and effectively treat Alzheimer's Disease by 2025, and to continue to develop a clear roadmap of research and treatment discovery priorities and timelines, we recommend that the interim research milestones first established in 2013 be evaluated and updated each year, to assure continuing and successful progress toward achievement of this goal**.
    - Interim milestones should develop and describe a continuing process by which research priorities aimed at accelerating the delivery of effective preventions and treatments are set and executed, including input from scientific experts from both academia and industry, and describing respective public and private roles reflecting the true partnership between government and industry needed to achieve our national goals.
    - The Administration should estimate the federal funding that will be required each year to successfully complete the interim milestones through completion of the 2025 research goal. Like the milestones themselves, these estimates should be revised annually, considering progress, emerging challenges and opportunities.
    - Given the fact that existing health disparities are likely to be a driving force in both the domestic and global efforts to combat AD, interim milestones should prioritize specific steps to reduce disparities in access to early diagnosis, costly diagnostic procedures, and potential disease modifying treatments, and to make significant improvements in recruitment and outreach to diverse populations, by racial/ethnic group, sex, and socioeconomic status, as well as populations at high risk for AD (e.g., people with Down Syndrome).
    - Interim milestones should include a plan to identify and rectify the shortcomings of the data needed to assess the prevalence, rates of diagnosis, costs (financial, fiscal and economic), and deaths relevant to Alzheimer's disease.
    - While the goal of making new remedies for AD available by 2025 is ambitious, it should not be interpreted as favoring translational drug development over basic discovery. 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 public and fiscal health.

2. **The urgent need for increased annual federal research funding sufficient to fund the strategic research plan reflected in the NIH milestones and to achieve the breakthroughs required to meet the 2025 goal remains a top priority. Initial estimates of that level are $2 billion per year but may be more. That investment would be applied to Alzheimer's research initiatives spanning basic, translational and clinical research**.

- The Administration, working with the research and business communities, should develop an overall budget needed to achieve the 2025 goal, and should propose to Congress and support a rapid ramp up to a minimum $2 billion in Alzheimer's research at NIH. The optimum levels of annual funding needed to achieve the 2025 goal should be determined in connection with the preparation of the President's budget, and should be reviewed and adjusted each year based on progress and new developments.
- We recommend that NIH coordinate with other federal agencies to ensure that overall federal Alzheimer's funding complements the NIH's investments and enhances progress towards the goal of preventing and effectively treating Alzheimer's by 2025. We also recommend that the strategic research plan identify and monitor not only existing resources within the Federal Government, but also new resources outside the Federal Government, including new private-public partnerships, incentives for increased private investment, state-based research funding, mobilization of global investments, and any other resources that may be generated by the innovative financing mechanisms described in the Path to 2025 Summit Report.

3. **Based on the recommendations of the 2013 ADRD Research Workshop, interim milestones for achieving specific research goals for the study of Alzheimer's Disease Related Disorders (i.e., Frontotemporal Degeneration (FTD), Lewy Body Dementia (LBD) and vascular contributions to ADRD) should be explicitly added to the National Plan**.

- This process can be initiated in the same way that data from the 2012 AD Research Summit was used to develop interim milestones for AD Research, by using the NINDS Council-approved, prioritized set of recommendations from the 2013 Alzheimer's Disease Related Disorders Scientific Workshop, and should include information about federal roles and responsibilities and the roles of other sectors in achieving such milestones.
- Recommendations from the ADRD Workshop should be used to develop specific set immediate (2014 - 2016), mid-term (2017 - 2020), and long-term (2021 - 2025) milestones to achieve the goal.
- We recommend that a follow-up ADRD Summit is held in 2016 in order to review and refine recommendations based on recent scientific discoveries.

4. **We recommend that HHS, in partnership with experts from the research community and industry, take steps to 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, by**:

- Advising and supporting the development of a reformed clinical trial process to reduce the duration of Alzheimer's clinical trials by up to two years, as recommended in the Path to 2025 Summit Report.
- Provide regulatory clarity with respect to the design, conduct, and analysis of AD trials (e.g., trial enrollment, endpoints, etc.), particularly in the pre-dementia stages of disease, through the finalization and discussion of a Guidance document.
- Use scientifically sound regulatory mechanisms as appropriate to help expedite the approval of effective therapies for AD and other dementias, including the Accelerated Approval process to potentially approve drugs for preclinical disease based on an effect on an intermediate clinical endpoint that is reasonably likely to predict ultimate clinical benefit to patients (with further post-approval studies required), granting of Fast Track status for development programs for drugs intended to treat Alzheimer's disease and other dementias, and/or granting a Breakthrough Therapy designation for development programs with compelling preliminary evidence of efficacy in these conditions.
- Actively engage in and facilitate AD related public/private partnerships to formally qualify both endpoints and biomarkers to help facilitate the conduct of AD trials, and help generate data standards that will help facilitate regulatory review as well as allow for the pooling of future trial data.
- Engage with patient communities and advocacy groups to help inform the regulatory decision making process.

5. **We recommend that the Administration build on the commitments issued at the G8 Dementia Summit in London on December 11, 2013 and take a leadership role in establishing a Global Alzheimer's Action Plan to respond to the global scope of the Alzheimer's challenge. We recommend that this response will include, among other strategies, the following**:

    a) A coordinated international research action plan,
    b) A coordinated clinical trial infrastructure for Alzheimer's, including linked patient registries, longitudinal studies and trial-ready patient cohorts,
    c) A global fund to increase collectively and significantly the funding for Alzheimer's research, and
    d) A policy framework designed to provide incentives for additional investment in Alzheimer's research, including improved harmonization of national and regional regulatory regimes regarding Alzheimer's diagnostic and therapeutic products.

- The responsibility for such an initiative would be the responsibility of the Office and officials in the White House recommended below (Recommendation 6) as well as the agencies and departments of the Administration responsible for health, foreign affairs and finance, among others. The Administration, in that regard, should consider the appointment of a Dementia Innovation Envoy with a similar charge to that appointed by the UK government.
- We urge the Administration to support, encourage and, with other governments and international bodies, cause to establish an International Advisory Council on Research, Care and Services composed of member nations from the G8, G20 and low and middle income countries and representative of the diversity of stakeholders in the Alzheimer's-serving communities. Such an International Advisory Council would provide advice and support for the effective design and execution of a Global Alzheimer's Action Plan.

6. **We recommend that the Administration designate a specific Office and officials within the White House with responsibility and accountability for effective implementation of, and timely, transparent reporting on, all aspects of the implementation of this National Alzheimer's Plan and of the commitments made by HHS at the G8 Dementia Summit, including any global action plan as it is developed**.

- The designated Office within the White House should be responsible for the adequate and effective monitoring of the execution of the National Plan and G8 commitments across all agencies of the Federal Government, including HHS, DOD, VA, IHS, State and Treasury.
- These officials will develop a system of accountability for and reporting with respect to the achievement of the US and G8 2025 goal based on quantifiable metrics and milestones with respect to the action steps and strategies in the National Plan and in follow up to the G8 commitments.
- We recommend that the designated White House official report on progress over the prior year in meeting the annual objectives, strategies and actions enumerated in the National Alzheimer's Plan and in subsequent G8 and other international global action plans, as well as providing a comprehensive, multi-year perspective, and mid-course corrective action steps, that are needed in order to meet the 2025 goal of this Plan.