Industry Working Group on Alzheimer's Disease

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The Honorable Kathleen Sebelius
Secretary
United States Department of Health and Human Services
Hubert H. Humphrey Building
200 Independence Avenue SW
Washington, DC 20201

VIA ELECTRONIC DELIVERY

Dear Secretary Sebelius:

As you refine the draft National Plan to Address Alzheimer's Disease, leading biopharmaceutical organizations engaged in Alzheimer's and dementia research and drug development are pleased to have this opportunity to offer comment on a strong first draft. The organizations participating in the Industry Working Group on Alzheimer's Disease (Working Group), identified above, represent many of the industry leaders striving to discover and develop therapies and diagnostics to prevent and treat Alzheimer's disease by 2025 if not sooner. We have collectively invested tens of billions of dollars and many decades of energy to change the course of Alzheimer's disease and dementia, and we are all too familiar with the scientific, medical, and financial challenges associated with this pursuit, as well as the human and societal costs. If we are to reach the HHS stated goal of preventing and effectively treating Alzheimer's disease by 2025 – which we support – nothing short of a transformational and transparent partnership between the public and private sectors will be required. We look forward to working with you to make this happen.

The immense risks and challenges associated with bringing a drug, biologic, or other therapies to market are well known. The 1 of every 10,000 potential therapies that end up being approved for patient use take on average 13 years and cost well beyond $1 billion each to develop. For Alzheimer's and dementia research, scientific and other challenges have resulted in a very small number of approved treatments. And of the medications currently available, they address only the symptoms of the disease.

As noted above, we strongly applaud you and the Advisory Council on Alzheimer's Research, Care and Services for embracing the bold and appropriate Goal number 1 of preventing and effectively treating Alzheimer's disease by 2025. Given the significant current public health and fiscal challenges – and the even greater looming health and fiscal threats posed by the disease – this is indeed an appropriate goal. Fifty years ago, the nation committed to sending a man to the moon within the decade. We believe the time has come for a second moon shot, one focused on preventing and treating Alzheimer's disease. Just as we succeeded in putting a man on the moon ahead of schedule, we believe this goal can be achieved if the right resources – public and private – and the right policies -- those that encourage and accelerate the development of safe and effective treatments – are brought to bear. The challenge before us now is how to achieve this goal.

This Working Group has devoted considerable time and energies studying this question and is pleased to offer the following comments and suggestions to maximize our collective abilities to achieve success. We have targeted our comments and recommendations within five core areas:

- Strengthening the role of industry in the overall process, particularly by providing continuing and dynamic input into determining our national research priorities and ways to compress the discovery pipeline.

- Providing greater specificity and detail – as well as an accurate statement of resources – that will be necessary to achieve the strategies and goals.

- Including the policy incentives necessary to attract and sustain robust industry and capital commitments to Alzheimer's and dementia research.

- Establishing metrics that are useful in driving the desired outcome, are clear, and are measurable.

- Extending our vision to encompass the global challenge presented by Alzheimer's disease and dementias.

We will comment on each overarching point and then offer a number of more specific comments and suggestions for the next draft of the National Plan.

I. Strengthen the role of industry in the overall process, particularly by providing continuing and dynamic input into determining our national research priorities and ways to compress the discovery pipeline.

We are encouraged to see multiple references from the Administration that this plan be a true National Plan rather than a federal plan, meaning that it will include shared rights, roles, and responsibilities for all stakeholders. To ensure this desire is achieved, the Working Group strongly believes that the next version of the plan **must include a more robust and ongoing process of partnership between government – particularly the National Institutes of Health and the Food and Drug Administration – and industry**.

For example, while we appreciate the upcoming NIH summit and the Request for Information to collect widespread input on the research agenda, we note these actions are limited to one-time occurrences and do not contemplate an ongoing and robust dialogue and exchange with industry partners. Also concerning is that other recommendations – including sets 1.B, 1.C, and 1.E, which are focused on expanding research, accelerating effort to identify early and pre-symptomatic stages of the disease, and compressing the discovery timeline, call for what may be viewed as token or no industry engagement whatsoever despite the immense value such involvement would bring to the larger effort.

Specifically, action 1.E.1 focuses on identifying ways to compress the time between target identification and release of treatment, but calls for industry to be involved only indirectly. **We strongly believe the plan should recognize an explicit role for industry with a direct seat at this and related tables given the predominant role we collectively play in the therapy discovery and development process.** In this way, together, we will begin to set a concrete course that characterizes a new, vital and transparent partnership between the public and private sectors, aligned to achieve the 2025 goal.

Beyond the points above, we urge that the draft plan be amended to include the following:

- **Commit to establishing a meaningful partnership with industry and an ongoing process of dialogue between industry and NIH and the National Institute on Aging (NIA) in determining research and related priorities.** Inviting industry to the table to identify significant areas of research need and to present perplexing questions in need of basic research will breathe life into the concept of life cycle innovation by providing invaluable input and exchange of ideas. If the government wants to create a truly national plan, we believe this new partnership with the private sector, one that is open, transparent, and ground-breaking, should be at the core of the plan. In terms of specific models, we recommend exploring the Forum for Collaborative HIV Research and related HIV/AIDS models as potential examples, as well as the platforms created through the Therapeutics for Rare and Neglected Diseases (TRND) program for industry engagement.

- **Establish a standing NIH/NIA and Industry Alzheimer's Working Group** to provide the institutes with the continuous feedback loop on research and drug discovery issues such as those raised above. One potential model may be the CEO Roundtable on Cancer, which involves a number of industry partners as well as governmental collaborators including the NIH and FDA. Such a partnership could provide the NIH and other federal entities not only with additional voices and input but also with potential resources to support initiatives, such as more regular scientific conferences and inventories.

- **Increase patient enrollment in clinical trials, particularly targeted minority patients.** We strongly applaud this aspect of the plan and we urge that industry play a meaningful role in crafting the recruitment action plan, including being consulted on the populations or sub-populations we believe are most in need. This action plan should include specific tools for attaining this increased participation, such as targeted patient registries.

II. Provide greater specificity and detail – as well as an accurate statement of resources – that will be necessary to achieve the strategies and goals.

The Working Group embraces many of the research action steps included in the first draft plan. Expanding basic research into the underpinnings of the disease, identifying risk and protective factors, identifying biomarkers, and identifying ways to compress the therapy development timeline are all tremendously important if we are to achieve the 2025 goal. But each of these strategies and actions is only as good as the corresponding action steps required to achieve them, and we believe greater specificity and detail than what is contained in the first draft is needed. **We also believe that given the enormity of the challenges before us, the plan must speak to the significant yet realistic financial resources – both public and private – that must be brought to bear against this disease to stop it from destroying our health and finances. You have been bold in stating the 2025 goal, so too you should be realistic in setting the expectation for the resources – and scope of investment across the public and private sectors – that will be required to meet this goal.**

Following are comments in terms of enhanced specificity that we feel would strengthen the plan.

A clear path to the validation of a family of diagnostic and predictive biomarkers

- Catalogue existing Alzheimer's biomarker initiatives including their focus/type *(e.g., inclusion, prognostic, surrogate endpoint)* and *where* they currently lie in terms of their development and review, identify gaps, and establish a plan that seeks to validate specific biomarkers within a certain timeframe.

- Convene a joint high-level meeting between FDA and European Medicines Agency (EMA) leadership focused on Alzheimer's biomarkers and surrogate endpoints – including imaging modalities and imaging agents – and the much-needed harmonization of guidance and approvals.

- Develop a joint NIH and FDA – in close consultation with industry – action plan focused specifically on identifying and validating Alzheimer's biomarkers. This will be a subset of the larger research prioritization and action plan and involve ongoing NIH, FDA and industry dialogue to better understand biomarker needs, to update the biomarkers action plan, and to provide clear and direct guidance to industry on the use of such tools.

- Engage the National Center for Advancing Translational Sciences (NCATS) on specific initiatives focused on biomarker and surrogate endpoint development and addressing challenges in conducting clinical trials in pre-symptomatic patient populations.

- Issue, upon biomarker and endpoint approval, unambiguous guidance to industry on their usage.

A reduction in the cost and time of clinical trials and clinical trial processes

- Create large-scale, open-architected patient registries, with a particular focus on ethnic subpopulations.

- Engage industry as to population and subpopulation engagement, data, and other needs.

- Consider the applicability of novel trial designs, such as models used to address rare disease, for Alzheimer's disease.

Improved access to standardized electronic health and clinical trial data

- Establish a process involving NIH, FDA, and industry to identify core data issues. Topics would include access to data – including intervention arm data, failed trial data, dormant therapy data, biomarker data and other valuable data sets – as well as agreeing to and extending the use of common data standards.

- As part of this process, engage with industry around specific ideas to enlarge the space of appropriate data sharing. Members of the Working Group have each participated in the Alzheimer's Disease Neuroimaging Initiative, in many ways a seminal effort to explore and expand this space. We understand the opportunities afforded by efforts such as these, both to accelerate development where signals are positive and to fail early where signals suggest a dead end. We are prepared to build on these experiences to create new models that serve to advance therapy development across the sector.

Honest assessment of the level of resources necessary to achieve the 2025 goal

- Include within the strategies and action items a realistic estimate of the resources necessary to achieve success, and a statement as to how the federal government, particularly during financially challenging times, plans to meet its commitment.

- Extension of the scope and scale of responses to the global scale including a path forward toward a global action plan and fund.

III. Include the policy incentives necessary to attract and sustain robust industry and capital commitments to Alzheimer's and dementia research

The draft national plan is deficient in that while it notes the importance of compressing the discovery timeline, it fails to mention financial and other policy levers that are needed to attract and sustain robust industry and capital commitment to this most challenging area of research. **We urge that you speak to the role of smart incentives within the draft plan and lay out a path for addressing these topics near-term.** Specific issues we recommend the plan address directly or develop a process involving industry stakeholders to address include:

- Maintaining and strengthening a patent system that encourages and rewards innovation and protects and provides a fair return on investment.

- Establishing avenues for the collaboration of the public and private sectors that realistically take into account the genuine needs and strengths of both groups.

- Ensuring appropriate payment for any successful therapy that takes into account the enormous costs of research and drug development in this critical area. This requires adequate federal reimbursement and payment policies and having the Center for Medicare & Medicaid Services (CMS) at the table whenever warranted.

IV. Establish metrics that are useful in driving the desired outcome, are clear, and are measurable.

The members of the Working Group strongly believe that meaningful and clear metrics and milestones are absolutely essential for implementing any plan and holding responsible parties accountable. In business, clear action plans and corresponding metrics are commonplace and indispensable in keeping projects focused, on schedule, and on budget. All three of these attributes are necessary if the National Alzheimer's Plan is to be successful in achieving its goals, but the current plan falls short in this area, particularly in setting outcomes for action items. For example:

- The draft plan seeks to increase enrollment in Alzheimer's clinical trials but fails to specify specific numbers, target demographics or interim milestones.

- It seeks to increase the pace of collaboration between the Departments of Health and Human Services and Veterans Affairs but does not provide a clear timeframe or goals.

- It seeks to identify biomarkers but does not establish targets or set a timeframe for biomarker acceptance and validation by the FDA.

- And it speaks to maximizing government and industry collaboration but does not espouse clear goals for this action, only events like meetings and conferences and high-level themes.

While all of these and other actions are meritorious, they require clear metrics and a commitment to aggressive oversight. To that end, the industry Working Group recommends that the plan be amended to:

- Commit to develop this year specific action steps and metrics for each action starting with the designation of a specific federal official/office to manage each action.

- Develop and post on the NAPA website a user-friendly "dashboard" to regularly track progress toward each action, strategy, and goal.

- Work with industry and other appropriate partners to establish metrics that will increase our collective ability to achieve our goals, particularly the goal of preventing and treating Alzheimer's by 2025.

V. Extend our vision to encompass the global challenge presented by Alzheimer's disease and dementias.

In a recent speech, Professor Peter Piot, former Under Secretary-General of the United Nations and former executive director of UNAIDS, called dementia "one of the largest neglected global health challenges of our generation" and called for a global health action plan to address it.[1] Alzheimer's disease is an epidemic that respects no national boundaries and that threatens to cripple the health and finances of the world if unaddressed. The statistics are clear: more than 36 million people worldwide currently have Alzheimer's or dementia, and projections estimate this number will skyrocket to 115 million by the mid-century point, according to Alzheimer's Disease International. The economic impact of the current epidemic exceeds $600 billion annually, and nearly two-thirds of all victims live in developing nations that are largely ill-equipped to address the challenge.[2]

Earlier this year, rating agency Standard & Poors issued an analysis that said "Population aging will lead to profound changes in economic growth prospects for countries around the world, we believe, as governments work to build budgets to face ever greater age-related spending needs."[3] If governments fail to address this challenge and amend their social benefits systems, the agency concluded, the systems will become unsustainable." As Professor Piot noted, we must learn from the global approach to combat HIV/AIDS and enact a similar approach to Alzheimer's and dementia. No single country can take on this massive and multi-faceted endeavor alone, and the United States should be forceful and positive in recognizing this.

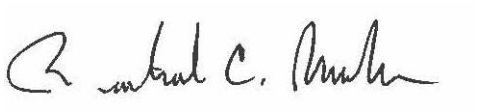
The draft plan acknowledges the need for greater collaboration between the U.S. and international partners, specifically Canada, the United Kingdom, and other nations that have or are developing National Alzheimer's Plans. This is a solid step that must be built upon with a clear path forward. Specifically, we urge that the global section be built out and contemplate specific measurable steps the U.S. will take to help develop and execute a global action plan as well as a global fund focused on both treatment and therapy development.

[1] See: http://alzheimers.org.uk/site/scripts/news_article.php?newsID=1169
[2] See: http://www.alz.co.uk/research/files/WorldAlzheimerReport2010.pdf
[3] See: http://www.standardandpoors.com/ratings/articles/en/us/?articleType=HTML&assetID=1245328578642

Conclusion:

Madame Secretary, the members of the ad hoc Industry Working Group wish to express our deep gratitude to you for taking meaningful actions to address our national and global Alzheimer's epidemic. We believe the draft National Plan to Address Alzheimer's Disease is a strong first step, and we offer the above comments and suggestions as part of a sincere offer to foster a true partnership and collaboration with you and your colleagues to prevent and treat this disease by 2025. We welcome any questions you may have, and we stand at the ready to discuss any of our comments with you and your team directly if desired.

Sincerely,



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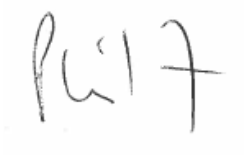

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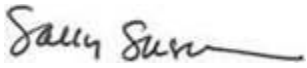

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