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May 8, 2015

The Honorable Fred Upton
Chairman
Committee on Energy & Commerce
2125 Rayburn House Office Building
Washington, DC 20515

The Honorable Frank Pallone
Ranking Member
Committee on Energy & Commerce
2322A Rayburn House Office Building
Washington, DC 20515

Dear Chairman Upton and Ranking Member Pallone:

As Founder and Chairman of USAgainstAlzheimer's, the leader in the national movement to stop Alzheimer's disease by 2020, I am writing to applaud your bipartisan leadership to advance the 21st Century Cures initiative. The latest draft reflects the tremendous commitment both of you have to developing this initiative in a bipartisan manner. You, your colleagues and staff members should be applauded for the amount of work expended over the past few months to refine and improve the concepts included in the discussion draft and produce this comprehensive draft legislation.

As the only leading disease that lacks both a means of prevention and any disease-modifying therapies or treatments, Alzheimer's disease and related dementias underscore the urgent need for a comprehensive re-envisioning of the policies that support discovery, development and delivery of therapies to those in need. USAgainstAlzheimer's strongly supports many of the provisions included in the latest draft. At the same time, we ask you to consider several ideas to further strengthen and enhance this legislation. For organizational purposes, we have divided our comments into two categories:

- 1) Research & Discovery; and
- 2) Accelerating Therapy Development & Review.

Overall, we believe that the latest draft and its bipartisan backing represent a major step forward, and we are pleased to work with the committee to advance this initiative.

I. Research & Discovery

Sec. 1001. NIH Reauthorization: We commend you for including an explicit reauthorization, including incremental improvements in funding levels, of the National Institutes of Health (NIH). While the funding levels are still far below where NIH must be to support even a quarter of meritorious research proposals it receives on an annual basis, the three-year funding authorization represents a sizeable step forward over what has been a flat or declining budget over much of the past decade-plus.

Sec. 1002. NIH Innovation Fund: We strongly applaud you for creating, authorizing and appropriating the 5-year NIH Innovation Fund. It is critical that funds appropriated under this section remain true to the core intent of Cures – to spur innovation and deliver improved therapies to patients far faster than we are doing today. As you continue to develop and refine this section, USAgainstAlzheimer’s urges you to **insert language that would target the Innovation Fund in part to high-risk, high-reward research to pursue areas of research with significant unmet medical need.** Such language would complement **Sec. 1028**, which would establish institute-level set-asides for high-risk and high-reward research, and would exemplify that Cures is focused on reforming the status quo to more aggressively develop and deliver treatments, therapies and cures. In doing so, USAgainstAlzheimer’s urges that the Fund be authorized to invest in clinical development and, specifically, to advance recruitment of patients into clinical trials and to advance the regulatory science of biomarkers. **We also recommend that you model the Innovation Fund on the Innovative Medicines Initiative (IMI) and require that project and program funding be matched by industry, academia, philanthropy or other sources.** Incorporating such a provision would create a true public-private partnership vehicle that would complement IMI and would serve as a “force multiplier” of the public commitment of \$10 billion over five years. We also recommend that similar to **Sec. 1026**, which would provide Other Transactional Authorities to the National Center for Advancing Translational Research (NCATS), you strongly consider providing such authorities to the Innovation Fund as well. Doing so will help ensure that the fund has both the resources and the authorities necessary to achieve innovation.

Sec. 1021. NIH Research Strategic Plan: USAgainstAlzheimer’s supports this provision. Research priorities can and do evolve over time. As such, it is critical that the NIH regularly review – in a comprehensive and transparent manner – the agency’s portfolio to ensure that scarce resources are being applied to the areas with the greatest levels of need, scientific opportunity and societal cost burden. We also strongly support the annual review to measure progress made against the plan and to course-correct, if necessary. While there are many examples of areas where a shift in both need, scientific opportunity and cost burden may warrant consideration of a strategic re-deployment of NIH resources, perhaps no area is this more apparent than in Alzheimer’s and dementia. While Congress and the Administration have both acted to increase the NIH commitment to Alzheimer’s research, this category still lags far below what is needed and what is being allocated to other diseases of lesser need, scientific opportunity and cost burden, particularly given the current and projected health and cost burdens of Alzheimer’s and the scientific opportunity before us today. The strategic plan would provide a mechanism for NIH to make transparent and accountable decisions on such issues.

Sec. 1027. NCATS Phase IIb Restrictions: We applaud the proposal to permit NCATS to support later-stage clinical research, which will allow NCATS to more fully perform its mission.

Secs. 1102 and 1121 – Standardization of Clinical Trial Data, Registry Data Bank and Clinical Trial Data System: Recruiting patients for Alzheimer’s and dementia clinical trials is a significant impediment to the development of Alzheimer’s therapies and treatments. USAgainstAlzheimer’s is leading multiple initiatives to address these barriers, which we will detail further in the next section. We strongly support standardizing data within ClinicalTrials.gov to facilitate participation in clinical trials. We also strongly support establishing a clinical trial data system to gather de-identified clinical trial data in one site. The number of Alzheimer’s disease trials that have been conducted over the past two decades could have provided researchers and industry with a true treasure trove of data that would be helpful in informing research targets and directions, trial designs and other research elements. And disclosure and pooling of clinical trial data from failed trials would permit the field to avoid repeating the testing, at great expense, of methods of action that had failed previously but where the failure was not known to others

in the field because of lack of disclosure. Collecting these data assures that generalizable knowledge is gained from the commitment made by the individual participants in clinical trials, a core ethical promise made to every patient who enrolls in a clinical trial. As you continue to develop and refine this section, it is crucial that any such database be open to qualified researchers, including medical product developers. We would also recommend that you consider establishing an advisory board that would include representatives from the patient, academic researcher and industry communities to advise on the design and deployment of this system to ensure it achieves maximum positive impact.

Sec. 1122. National Neurological Diseases Surveillance System: Research issued last year by a team from Rush University underscored the dramatic under-counting of deaths attributable to Alzheimer's disease each year. While inaccurate completion of death certificates is a cause of this problem, more detailed surveillance and tracking of neurological disorders including Alzheimer's and dementia would also be helpful to better understand the full extent of this disease on our population. As such, we encourage you to retain this section and urge you to include "Alzheimer's and related dementias" as conditions that would be included within this surveillance system.

II. Accelerating Therapy Development & Review

Sec. 1141. Council for 21st Century Cures: We applaud you for establishing the council and for providing it (and, we suggest, the Innovation Fund) with the authority to identify opportunities for collaboration with the Innovative Medicines Initiative (IMI) and other similar entities located outside of the United States. We encourage you to further strengthen this provision to allow not only the identification of such opportunities but also recommendations as to specific undertakings that should be supported by NIH, the Food and Drug Administration (FDA) or other government agencies. We also recommend that the external members of the board be adjusted to include representatives from business and industry beyond the biopharmaceutical, medical device and related industries. This would reflect the reality that our nation's employers foot much of the bill for health care costs and other challenges related to disease and ill-health, and would also bring potentially valuable business perspectives from outside of the healthcare sector to the table. We also urge you to retain Sec.281D(b) permitting and encouraging the council to accept financial or in-kind support from the private sector when deemed appropriate.

We have witnessed first-hand the tremendous potential possible through operating models like the IMI. In March, a project known as the Global Alzheimer's Platform being led by USAgainstAlzheimer's entered into an agreement with IMI to form a global, standing and trial-ready Alzheimer's drug development platform. This is intended to address head-on our challenges with clinical trials, particularly the lengthy start-up times and costs involved in such work. Public funding from the European Union as well as industry funding have contributed to this groundbreaking project. While we are making progress, the absence of an IMI-like entity in the United States today makes this effort more complicated and challenging to execute.

Sec. 2001. Patient Experience Data: As a network of patients, caregivers and other stakeholders committed to stopping Alzheimer's, USAgainstAlzheimer's believes strongly in patient empowerment and in the potential of Patient-Focused Drug Development (PFDD) writ large. We support the inclusion of data collected by caregivers within the definition of Patient Experience Data given how Alzheimer's and dementia rob the patient of his or her ability to fully participate in such processes. We urge that you retain these important caregiver references in this provision and that you look for other ways to include the voice of the caregiver as well as the patient within PFDD tools and authorities.

Sec. 2021. Qualification and Use of Drug Development Tools: USAgainstAlzheimer's agrees that the absence of biomarker endpoints for assessing the effectiveness of new molecular entities is a significant barrier to patients seeking speedier access to innovative medicines. This is particularly the case for Alzheimer's and other dementias as the field seeks to test potential preventive medicines in preclinical populations before any disease symptoms appear. Identifying a biomarker on which a new endpoint can be based because it is predictive of disease progression is a challenge of both science and regulation. Obtaining the data from companies that would provide the evidence needed to determine the predictive efficacy of a biomarker has been a challenge. USAgainstAlzheimer's urges that any effort to regulate the regulator in this area be accompanied by incentives to companies, and potential authorities to the FDA, that would result in the sharing of biomarker evidence obtained in industry-sponsored clinical trials and studies so the needed scientific basis for evaluating the predictive efficacy of a biomarker can be firmly established. In the experience of USAgainstAlzheimer's, regulators are prepared to approve biomarker endpoints if the scientific basis for doing so is presented.

Secs. 2061 – 2063: Clinical Trial Design Modernization: As noted earlier, the time, cost and risk of the clinical trial process has been a significant barrier to innovative medicine development in Alzheimer's. In particular, the recruitment of patients to Alzheimer's clinical trials and the overall logistics, costs and other resources associated with setting up repetitive, sequential trials on a one-off basis have been a major disincentive to investment. We are encouraged by provisions intended to modernize clinical trials to better leverage the advanced computing and other technologies of today and tomorrow to reduce trial length and cost while still ensuring patient safety and product efficacy. More adaptive trials design models must be tools in the present-day drug development toolbox, and guidance from the FDA on how such tools can be designed and used is necessary. Additionally, particularly in areas like Alzheimer's, with profound unmet medical needs, it makes sense to pursue other sources of evidence, including post-approval clinical experience data, so that patients in need could obtain access to therapies as soon as practicable and, in the case of a terminal disease like Alzheimer's, before it is too late.

Secs. 2082-2083: Expanded Access: We support the provision to require additional details from medical product manufacturers regarding their policies with regard to expanded access or compassionate use of investigational products. Vital details such as company points of contact, procedures and criteria for such requests and estimated timeframes are important for patients and their healthcare providers who may be contemplating such requests. We also welcome the call for further agency guidance on this important topic.

Incentives to Encourage Therapy Development: We recognize the many questions and challenges on the topic of appropriate incentives to attract and retain industry commitment to targeted therapeutic areas while at the same time promoting patient access to therapies. We know that incentive provisions have been a key topic of your negotiations over the past several months and recognize that a number of gaps, particularly in the areas of repurposing drugs for serious and life-threatening diseases and conditions, remain. We understand that the scientific challenges of Alzheimer's and dementia, the multiple late-stage failures over the past two decades and the high costs and lengthy timelines necessary for trials in the space have combined to dampen industry interest in the space. As such, we encourage you to continue your discussions on these topics, particularly to address in a meaningful way conditions like Alzheimer's and dementia that have profound unmet medical needs, well-recognized scientific challenges and lengthy clinical trials and other costs. We strongly believe that appropriately targeted incentives can be crafted in a way that would complement our national goal of preventing and effectively treating Alzheimer's disease by 2025 and that could limit government exposure through various tools such as sliding scales, caps and sunsets while providing a meaningful incentive to industry.

Given the experience with the Orphan Drug Act, USAgainstAlzheimer's believes there is strong evidence that properly-tailored incentives can produce positive results for patients in need.

Sec. 2241. Streamline the Institutional Review Board Process: This initiative recognizes that a number of Institutional Review Board (IRB) models exist and should be considered for use more broadly to help expedite and streamline the clinical trials process. We strongly support this provision given our experience in the Alzheimer's trials space, particularly the use of multi-site and multi-national clinical trials. We would welcome the issuance of regulations and guidance on the uses and roles of joint or shared reviews, independent or third party IRBs, centralized or federated IRBs and other models and arrangements that can reduce the time and administrative burden of starting new trials or, in the case of Alzheimer's, operating to maximum effect a global standing clinical trial platform now being developed by USAgainstAlzheimer's and the Innovative Medicines Initiative noted above.

Comments on Changes to the Draft & On Provisions Not Currently Included

Chronic Disease Longitudinal Study: We wish to thank you for heeding the concerns of USAgainstAlzheimer's and many other stakeholders regarding the chronic disease longitudinal study. Given the many pressing needs and research priorities before us today, we did not believe that such a project represents the best use of scarce resources. We were also concerned about potential duplication of existing Alzheimer's studies, about the potential negative impact such a study could have on clinical trials recruitment and on the pitfalls of such studies given the challenges experienced by National Children's Study. As such, we thank you for heeding these concerns and for removing this provision.

A Global Neurodegenerative Disease Clinical Trials Network: Much progress has occurred in this area since the first draft bill was released via the Global Alzheimer's Platform, described earlier, to create a global, standing and trial-ready Alzheimer's drug development platform in partnership with the Innovative Medicines Initiative. This is intended to address head-on our challenges with clinical trials, particularly the lengthy start-up times and costs involved in such work. While this project is moving forward and enjoys the support of the FDA and the NIH, **we urge you to take action to encourage US participation in the project by adding a provision similar to the Sense of Congress included as Sec. 1082 but focused on a global neurodegenerative disease clinical trials network.** Such an action would be particularly appropriate because the Alzheimer's network would present a prototype that could be used to accelerate clinical trials in other neurodegenerative conditions.

Thank you, again, for your tremendous leadership and efforts that have gotten us to this point. We greatly appreciate all you have done, and we urge you to consider incorporating this feedback within the next iteration of the draft. If you have any questions, or if you would like to discuss any of these ideas further, please feel free to reach out to me at any time.

Sincerely,



George Vradenburg
Founder and Chairman