NATIONAL HEMOPHILIA FOUNDATION
www.hemophilia.org

June 13, 2014

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

The Honorable Diana DeGette
Member
House Energy and Commerce Committee
2125 Rayburn House Office Building
Washington, DC 20515

Sent via e-mail: Cures@house.mail.gov

Re: Request for Information (RFI) Regarding the 21st Century Cures Initiative

Dear Chairman Upton and Representative DeGette:

The National Hemophilia Foundation, the nation's leading advocacy organization working on behalf of individuals affected by hemophilia and related bleeding disorders, appreciates the opportunity to submit these comments in response to the request for information from the patient community as part of the Committee's 21st Century Cures Initiative. Thank you for including consideration of financial burden on patients as part of your initiative. Indeed, ensuring that patients can access treatments once they are on the market is a key component of accelerating the cycle of discovery, development and delivery.

For this reason, we urge the Committee to move forward in considering HR 460, the Patients Access to Treatment Act. We have joined with many others in the Coalition for Accessible Treatments to endorse this legislation to increase access to life-saving drugs by removing the burden of excessive cost-sharing. HR 460 benefits people with bleeding disorders, and others with high-cost chronic conditions, such as leukemia and lymphoma, multiple sclerosis, rheumatoid and psoriatic arthritis, lupus, primary immunodeficiency diseases, and Crohn's disease.

Hemophilia is a rare, chronic bleeding disorder affecting more than 20,000 people in the United States, who infuse high-cost clotting factor therapies to replace missing or deficient blood proteins. Clotting factor therapies are safe, very effective, and allow people to lead healthy, productive lives. However, the financial burden of these life-saving therapies can be tremendous. Drug costs for a person with severe hemophilia can be $250,000 a year or more. Developing an inhibitor (an immune response to treatment), complications such as HIV/AIDS, hepatitis and joint diseases, or bleeding as a result of trauma or surgery can increase those costs to $1 million.

Given these costs, insurance specialty tiers that require individuals to pay for a percentage of their drug's cost mean that the expense of simply maintaining health can be financially crippling. Plans require higher patient cost-sharing for drugs and biologics as a tool to reduce utilization and incentivize patients to choose lower-cost generic alternatives. However, there are no generic alternatives to clotting factor therapies.

The use of specialty tier practices places medically necessary treatments out of reach of most Americans. Individuals with bleeding disorders who cannot afford specialty tier pricing are likely to delay or go without treatment, resulting in disability and other complications that can lead to increased

long-term health care costs. While the out-of-pocket max instituted by the Affordable Care Act allows families to predict what their health expenses will be in a given year, people with bleeding disorders are likely to hit their max in the first month or two of the year. It can be extremely challenging for individuals or families to afford to pay $6,350 or $12,700 in only a month.

The Energy and Commerce Committee could do much to incentivize innovation and improve the lives of people with bleeding disorders and many other conditions by passing HR 460 and ensuring patient access to life-saving, innovative therapies. We are happy to provide you with any additional information you may require. This is a critically important issue for individuals with bleeding disorders. The individuals we serve are anxious for your Committee to consider the bill so that it can move closer to enactment.

Sincerely,

Val Bias
Chief Executive Officer
National Hemophilia Foundation

cc: The Honorable David B. McKinley, United States House of Representatives
The Honorable Lois Capps, United States House of Representatives

June 13, 2014

The Honorable Fred Upton
Chairman
Energy and Commerce Committee
United States House of Representatives

The Honorable Diana DeGette
Senior Member
Energy and Commerce Committee
United States House of Representatives

Dear Chairman Upton, Congresswoman DeGette, and all members of the 21st Century Cures Initiative:

The Ovarian Cancer National Alliance (hereafter, the Alliance) applauds the goals of the 21st Century Cures Initiative and supports your efforts to bring biomedical research and the development of effective treatments to the forefront of Congress's attention. We greatly appreciate the opportunity to submit comments in response to your third white paper detailing the perspectives, concerns, and priorities of the ovarian cancer patient community.

The Alliance is an ovarian cancer survivor-led national organization that unites 58 state and local partner member organizations, grassroots activists, women's health advocates and health care professionals. The Alliance advocates at a national level for greater investment in federal research to support the development of an early detection test, improved health care practices and life-saving treatments. The Alliance also educates health care professionals about – and raises public awareness of – risk factors for and symptoms of ovarian cancer.

Summary of the Alliance's Recommendations

- Ensure steady and predictable funding, pegged to inflation, for biomedical research within the NIH, DoD, CDC and other agencies.
- Promote ovarian cancer prevention by ensuring the USPSTF has the statutory authority it needs to examine and grade effective interventions for all populations.
- Ensure that patients have access to all oncology drugs prescribed by their physician.
- Support smaller, smarter clinical trial design and incentivize the use of healthcare information technology in comparative effectiveness research.
- Support policies that ensure all women diagnosed with ovarian cancer receive the best possible care which adheres to national guidelines.

Introduction

Ovarian cancer is one of the deadliest cancers and accounts for three percent of all cancer deaths among women, despite affecting only a small number of women. According to the American Cancer Society, this year an estimated 21,980 women in the United States will receive a diagnosis of ovarian cancer and 14,270 women will die from this terrible disease[1]. A full quarter of women diagnosed with ovarian cancer will lose their fight to the disease within one year of their diagnosis and over half will die within five years. Unfortunately, survival rates for ovarian cancer have changed very little over the past 40 years[2].

The reason for these grim statistics is that there is no early detection test for ovarian cancer. Tragically, fewer than 15 percent of cases of ovarian cancer are diagnosed early, with the majority being caught only after the disease has begun to spread and is more difficult to effectively treat[3]. However, when ovarian cancer is caught in its earliest stages, over 93% of women survive more than five years[4]. As such, it is critical that women and health care providers be aware of the signs and symptoms of ovarian cancer and that valid and reliable early detection tests be developed.

Ovarian cancer patients also have access to scant few treatment options that have been approved by the Food and Drug Administration (FDA). Many FDA approved drugs are platinum-based therapies, to which cancers readily become resistant if multiple rounds of chemotherapy are needed. Nearly 80 percent of ovarian cancer patients will have a recurrence of disease, underscoring the great need for new and better treatments for ovarian cancer[5]. Implicit in the need for more treatments is the need for federal investment in the research necessary for their development.

Finally, a diagnosis of ovarian cancer places a tremendous financial burden on a patient and her family. Ovarian cancer is one of the most expensive cancers to treat. The National Cancer Institute (NCI) estimates that the first year of ovarian cancer treatment costs $82,324 per patient, a year of continuing treatment costs $8,296, and treatment for the final year of a patient's life costs $99,715[6]. By comparison, the average cost of breast cancer treatment is $23,078 in the first

[1] American Cancer Society. Available at: http://www.cancer.org/cancer/ovariancancer/detailedguide/ovarian-cancer-key-statistics

[2] The five year survival rate in 1975 was 33.6% and has only risen to 44.6% today. Statistics via the National Cancer Institute. Available at: http://seer.cancer.gov/statfacts/html/ovary.html

[3] Ibid

[4] Ibid

[5] National Cancer Institute. Available at: http://www.cancer.gov/cancertopics/pdq/treatment/ovarianepithelial/HealthProfessional/page6

[6] National Cancer Institute. Available at: http://costprojections.cancer.gov/annual.costs.html

year, $2,207 to continue, and $62,856 in the last year of life[7]. These figures only account for the direct costs of a woman's medical care, and do not include the considerable economic impact of lost productivity and premature death[8]. Any investment which prevents ovarian cancer or allows patients to be diagnosed earlier will clearly pay off in spades.

Harnessing the Power of the Ovarian Cancer Community

As the foremost advocacy organization for women with ovarian cancer, the Alliance acts to convene and leverage the ovarian cancer community to advance the research enterprise. Members of our community serve as patient research advocates on grant review committees, promote clinical trial patient accrual and disseminate the results of research studies.

To ensure that the patient voice is heard when research agendas are being set, drugs are being considered for approval, and trials are being designed, the Alliance trains and nominates survivors to serve as patient research advocates in various capacities. Roles for patients include reviewing grant proposals and setting research agendas as "Consumer Reviewers" for the DoD OCRP, reviewing and recommending new cancer drugs as patient advocates on FDA oncology drug advisory committees, ensuring that research protocols treat research participants fairly as members of Institutional Review Boards (IRBs), and providing the patient voice in clinical trial design as patient advocates in cooperative clinical trial networks. Over its 17 years history, the Alliance has been proud to nominate more than 20 women to serve in this capacity and continues to recruit and train the next generation of advocates.

For the past 17 years, the Alliance has convened its annual Ovarian Cancer National Conference, the largest conference on ovarian cancer for patients, caregivers, and their families. Conference speakers routinely include experts in ovarian cancer sharing the latest information about research and clinical trials. These conferences serve as a catalyst for patient involvement in the research enterprise, either through participation in clinical research, active engagement in research advocacy, or merely through connecting with other women to interpret and share research information.

New Diagnostics and Treatments for Ovarian Cancer: From the Bench to Bedside

Sustained, predictable and robust federal investment in ovarian cancer research is absolutely critical to the development of novel diagnostics and therapies for ovarian cancer. Many of the recent success stories in ovarian cancer – of which there are too few – are due in no small part to

[7] Ibid

[8] A 2009 American Cancer Society study estimated the yearly economic impact of cancer of $130 billion in indirect mortality costs. The same year, an estimated 585,720 US residents died of ovarian cancer, correlating to over $220,000 in impact per death. Available at: http://www.cancer.org/cancer/cancerbasics/economic-impact-of-cancer

federal funding. For example, in 2003, investigators at Johns Hopkins School of Medicine, funded by the Department of Defense (DoD) Ovarian Cancer Research Program (OCRP), identified five new biomarkers associated with ovarian cancer. By 2009, they had developed those biomarkers into a test that can screen women with an abdominal mass suspected to be ovarian cancer to refer them for specialized ovarian cancer care. That test, named OVA-1 and now offered by Vermillion, has FDA approval and is part of clinical practice guidelines.

Likewise, federal investment from the NCI was critical in the early development of a class of drugs called PARP inhibitors, which show great promise for treating women with breast and ovarian cancer related to *BRCA* mutations. Later this summer, AstraZeneca's olaparib, a PARP inhibitor, will undergo accelerated review by the FDA. However, only 15% of women with ovarian cancer have *BRCA* mutations and are candidates for PARP inhibitor therapy, leaving the vast majority of those with the disease with only traditional platinum-based therapies[9]. Clearly more research funding is necessary so all women with ovarian cancer can eventually benefit from the promise of personalized medicine.

Furthermore, NCI recently launched the National Clinical Trials Network (NCTN), which consolidates and streamlines existing cooperative clinical trial groups. One of these new groups, the NRG Oncology Clinical Trial network, includes the Gynecologic Oncology Group (GOG), whose trials have been responsible for several advances in ovarian cancer research. Specifically, a GOG trial found that chemotherapy followed by maintenance use of Avastin increased progression free survival time of advanced ovarian cancer patients, when compared to chemotherapy alone. By funding important trials such as this, GOG (and now NRG) fills a clinical research gap left open by pharmaceutical companies that do not often research maintenance or combination therapies. Due to the NCTN's critical importance in clinical trial design and implementation, robust NCI funding is necessary to accomplish these and other important tasks.

Commented [LK1]: It's a messy acronym to define. From their website:

NRG Oncology brings together the unique and complementary research areas of the National Surgical Adjuvant Breast and Bowel Project (NSABP), the Radiation Therapy Oncology Group (RTOG), and the Gynecologic Oncology Group (GOG).

In FY2013, the United States government funded nearly $166 million in ovarian cancer research and education programing through the OCRP, NIH and Centers for Disease Control and Prevention. The next largest private funder of ovarian cancer research, the Ovarian Cancer Research Fund, was only able to award approximately $6 million in grants. Clearly, federal research dollars are the life blood of the ovarian cancer research enterprise. The Alliance urges Congress to maintain a strong commitment to funding biomedical research with steady, predictable funding keeping pace with inflation.

A Role for Congress in Advancing the Prevention of Ovarian Cancer

[9] Pal, T. et al. (2005). *BRCA1* and *BRCA2* mutations account for a large proportion of ovarian carcinoma cases. *Cancer*. 104: 2807 – 2816.

It is estimated that one in five cases of ovarian cancer are caused by inherited genetic mutations in *BRCA* and other genes[10]. Women with hereditary ovarian cancer may be at risk of developing additional cancers[11] and may be eligible for new targeted therapeutics currently in clinical trials[12]. In this light, the Society of Gynecologic Oncology (SGO), recently issued a recommendation that all women diagnosed with ovarian cancer undergo testing for *BRCA* and other genetic changes[13].

The United States Preventative Services Task Force (USPSTF) has given *BRCA* testing a "B" rating for women with high risk of developing breast and ovarian cancer, as evidenced by a family history of disease. Under this rating, qualifying women can receive genetic counseling and *BRCA* testing with no out of pocket cost. However, this recommendation does not extend to women who have previously been diagnosed with breast or ovarian cancer – meaning these patients may have to pay out of pocket for the testing.

The Alliance has called upon the USPSTF to extend these recommendations to women currently diagnosed with breast of ovarian cancer. Women may choose to use the results of their genetic testing in the decision to undergo a prophylactic mastectomy or salpingo-oophorectomy (removal of the ovaries and fallopian tubes) in order to prevent a future cancer. They further may choose to change their reproductive plans based upon their testing results or alert members of their family about the risk they may potentially share. Furthermore, expanding genetic testing is consistent with SGO's clinical practice recommendations urging testing of all women with ovarian cancer. At this time, USPSTF has not chosen to expand its list of eligible populations.

We urge Congress to ensure that there are no statutory limitations preventing the USPSTF from recommending expanded *BRCA* testing and genetic counseling for women currently diagnosed with cancer. Any such limitation is inconsistent with the science supporting increased testing and the spirit of the Task Force's mission of prevention.

A Role for Congress in Advancing the Treatment of Ovarian Cancer

As discussed previously, there are far too few FDA approved therapeutics for ovarian cancer. There are several reasons for this, two of which will be discussed in detail below: (1) some drugs

[10] Kanchi et al. (2014). Integrated analysis of germline and somatic variants in ovarian cancer. Nature Communications. 5: 3156.
[11] Women with mutations in the *BRCA* genes have up to an 80 percent risk of developing breast cancer, a 40 percent risk of developing ovarian cancers and a slightly elevated risk of colon cancer. Men who carry *BRCA* mutations have an increased risk of prostate cancer.
[12] A new class of drugs called PARP inhibitors appear to be effective in treating cancers caused by *BRCA* mutations.
[13] SGO Clinical Practice Statement: Genetic Testing for Ovarian Cancer. March 2014. Available at: www.sgo.org/clinical-practice/guidelines/genetic-testing-for-ovarian-cancer/

commonly used "off label" for ovarian cancer treatment and (2) clinical trials are difficult to design and complete due to a small patient population and high morbidity rate.

Off-Label Use: As is common in many oncology settings, ovarian cancer patients often receive "off label" therapies. These therapies have been determined to be safe through FDA review, are medically-accepted (often appearing in clinical practice guidelines) and potentially life-saving. Yet as they lack a label indication for use in ovarian cancer, payers are not required to reimburse for their use despite being ordered by a physician. For example, the drug Avastin is covered by CMS because it appears on compendium guidelines for ovarian cancer. However, in 2011 patients in Oklahoma, New Mexico, Colorado, and Texas were denied access to the Avastin because the Medicare contractor in that jurisdiction refused to reimburse for "off label" use of the drugs. This policy was later reversed, thanks to the action of 43 Members of Congress, but prior to its reversal many women were left without access to drugs they needed for their treatment[14]. The Alliance urges Congress to support policies that ensure all Medicare beneficiaries have the same access to therapeutics ordered by their doctors.

Clinical Trial Design: Clinical trials are difficult in ovarian cancer due to low enrollment rates, a small patient population and high disease mortality rates. These factors lead to low incentives for pharmaceutical companies to invest in ovarian cancer trials. For these reasons, federally funded clinical trials, such as those run through the NRG Oncology cooperative group mentioned above, are critically important in ovarian cancer and require robust investment.

Furthermore, as personalized medicine and targeted therapies become an increasingly larger portion of the drugs used in oncology, clinical trials design must change. Smaller and smarter clinical trials that can pool a limited number of patients with ovarian cancer and match them to targeted therapies based on the genetics of their tumor will be critical in bringing about these changes. These type of clinical trials already exist for some other diseases – notably the I-SPY2 trial in breast cancer and Master Protocol in lung cancer – and have received enthusiastic support by the FDA. The Alliance applauds these efforts and hopes that Congress will continue to encourage their development and expansion to other diseases, such as ovarian cancer.

Finally, we believe that Congress should incentivize the use of health information technology and comparative effectiveness research in drug evaluation. The creation of a centralized, interoperable patient data registry that tracks both traditional and patient reported outcomes, drug utilization, and adverse events will be critical in evaluating novel and existing therapies for ovarian cancer.

[14] Ovarian Cancer National Alliance. February 3, 2011. Update on Medicare Coverage for Avastin (bevacizumab). Available at: www.ovariancancer.org/2011/02/03/update-on-medicare-coverage-for-avastin-bevacizumab/

Ensuring all Patients Receive Standard of Care in Ovarian Cancer

Recent research studies show that the majority of women do not receive standard of care in ovarian cancer treatment. A study last year found that only 37 percent of patients treated for ovarian cancer in California had their primary surgery done by a specialist and were treated with the correct chemotherapy regime[15]. Further data presented at the 2014 meeting of the American Society of Clinical Oncologists suggests this is also true in Medicare populations – where only 56 percent of patients received both surgery and chemotherapy. Strikingly, the same data showed that 11 percent of Medicare patients diagnosed with ovarian cancer between 2002 and 2009 did not receive either chemotherapy or surgery[16]. In a situation like ovarian cancer, where outcomes are so poor, we must ensure that we are using the few instruments – however blunt they may be – to treat patients in the most efficient way possible. We strongly urge Congress to support reimbursement and payment policies that promote healthcare provider adherence to quality measures defined by national treatment guidelines.

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Once again, we thank you for your leadership on this issue and the Committee for its attention. We hope that our comments and recommendations are helpful in bringing about a new future in the treatment of ovarian cancer.

Sincerely,

[redacted]

Calaneet Balas
CEO
Ovarian Cancer National Alliance

[15] Bristow et al. (2013). Adherence to Treatment Guidelines for Ovarian Cancer as a Measure of Quality Care. *Obstetrics and Gynecology*. 121: 1226-1234.
[16] Data presented by Dr. Larissa Meyer of MD Anderson.

Parkinson's Action Network

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Amy Comstock Rick, J.D.
Chief Executive Officer

June 13, 2014

The Honorable Fred Upton
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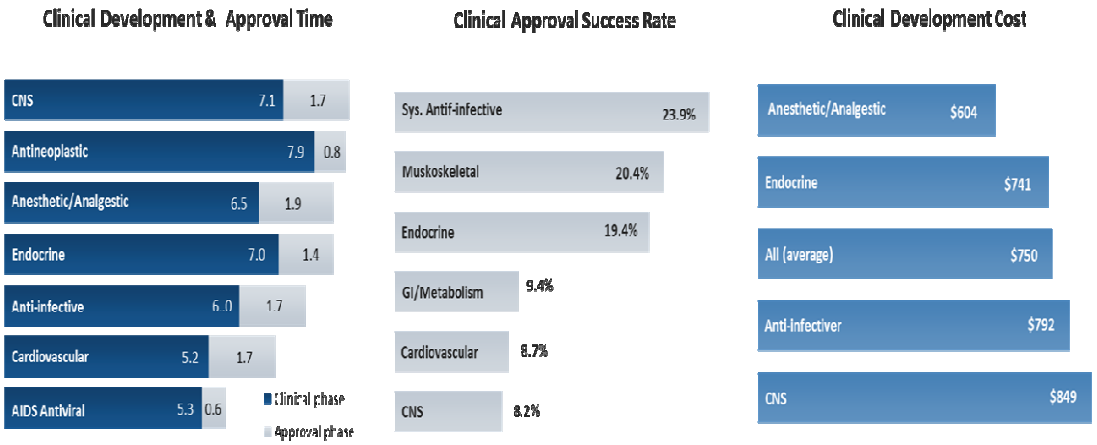
Washington, DC 20515

Dear Chairman Upton,

On behalf of the Parkinson's community, the Parkinson's Action Network (PAN) thanks you for your leadership on Parkinson's disease and for launching the 21st Century Cures Initiative to improve the discovery, development, and delivery of new treatments and cures for Americans.

We welcome the opportunity to comment on the 21st Century Cures "Patients" whitepaper, which seeks information on the state of biomedical research and therapeutic innovation for specific diseases and how Congress can help move the ball forward. As a community, we are enthusiastic about our prospects for the development of new therapies for Parkinson's and believe that the scientific community is close to developing the tools we need to fight this disease. However, we are concerned that the current system lacks the incentives for industry to invest and move targets through the pipeline for unmet medical needs of the central nervous system (CNS). In fact, data articulated in the chart below show that the process to develop drugs to treat CNS conditions, including Parkinson's, takes longer, is most costly, and has higher failure rates than the development process for drugs to treat other conditions. Accordingly, industry has shifted investment away from treatments for CNS diseases and conditions, further exacerbating this situation.



Source: Science, July 2010

It is from this perspective that we respond to your questions, outline the state of Parkinson's disease research and treatment, and provide recommendations for your consideration. Ultimately, we want to ensure that we level the playing field for CNS science and ensure that bright ideas are not abandoned because of business prospects

but are invested in and brought through the development process to achieve the greatest potential the science has to offer. We must look at alternative ways to further scientific discovery, decrease development time and costs as well as increase success rates for CNS diseases.

Progress towards Parkinson's Disease Treatments and a Cure

Parkinson's disease is the second-most common neurodegenerative disorder in the United States after Alzheimer's disease. National prevalence data is scarce but it is estimated that between 500,000 to 1.5 million Americans are living with the disease.

Current treatment for Parkinson's is based around a nearly 50-year-old pharmaceutical therapy, which treats only some symptoms for a limited period, generally four to eight years, and often with limiting side-effects. Eventually the medications lose their effectiveness, leaving the person unable to move, speak, or swallow. Deep Brain Stimulation, a surgical option used to treat symptoms, is not an option for everyone, and ultimately does nothing to stop the progression of disease. In fact, no existing therapies have been shown to slow or stop its progression. By far, the greatest challenge facing the Parkinson's community today is the lack of disease modifying therapies to slow or stop the progression of the disease.

A recent report released by the Pharmaceutical Research and Manufacturers of America (PhRMA) outlines 37 new Parkinson's disease drugs either in clinical trials or awaiting review by the Food and Drug Administration (FDA).[1] Some examples of potential advances in the report include:

- A gene therapy that targets the part of the brain that controls movement;
- A new medicine that targets a receptor found in the brain where degeneration and abnormality are often seen in Parkinson's disease; and
- New delivery mechanisms of approved treatments, including an intranasal formulation and an intestinal gel.

However, the number of new drugs is not as important as whether these medications are ultimately effective in improving the quality of life for people with Parkinson's. Much scientific work still needs to be accomplished to understand why people develop the disease, how to better treat symptoms that have no treatments, and ultimately find a way to slow or stop progression of the disease.

Financial Burden of Parkinson's Disease

A study published in 2013 in *Movement Disorders* estimated that the economic burden of Parkinson's disease is currently at least $14.4 billion a year in the United States, and the prevalence will more than double by the year 2040.[2] In addition, the study went on to find:

- Those with Parkinson's disease incurred Parkinson's-related medical expenses of $22,800 per patient annually -- $12,800 higher than someone without Parkinson's.
- Approximately 57% of excess medical cost is associated with higher use of nursing home services.
- The Parkinson's population incurred approximately 1.9 million hospital inpatient days in 2010, 73% more than would be expected for a similar population without Parkinson's disease.
- Excess health-care use attributed to Parkinson's disease in 2010 includes 1.26 million physician office visits, 57,000 outpatient visits, 31,000 emergency visits, 24,000 home health days, and 26,000 hospice days.
- The study calculated an additional $6.3 billion in indirect costs such as missed work or loss of a job for the patient or family member who is helping with care, long-distance to see a neurologist or movement disorder specialist, as well as costs for home modifications, adult day care, and personal care aides.

[1] Pharmaceutical Research and Manufacturers of America, 2014 Medicines in Development: Parkinson's Disease Report, April 2014, http://www.phrma.org/sites/default/files/pdf/2014-parkinsons-report.pdf.

[2] "The Current and Projected Economic Burden of Parkinson's Disease in the United States," *Movement Disorders*, Vol. 28, No. 3, 311-18. 2013.

A second study also published in *Movement Disorders* in 2013 projected that if Parkinson's progression were slowed by 50 percent, there would be a 35 percent reduction in excess costs, representing a dramatic reduction in cost of care spread over a longer expected survival.[3] Both studies highlight the enormous economic implications of this devastating disease, and make it abundantly clear that smart investment in medical research could significantly lower reliance on Medicare and Medicaid as a safety net for people with Parkinson's.

Public Funding for Parkinson's Research

While private Parkinson's disease foundations are funding important research and support programs, the federal government continues to play a pivotal and vital role in funding research and development of new treatments for Parkinson's disease. Currently, the National Institutes of Health (NIH) funds approximately $135 million (FY 2013) in Parkinson's basic, translational, and clinical science. There is a concerted effort at NIH to identify Parkinson's research opportunities. In January 2014, the National Institute of Neurological Disorders and Stroke (NINDS) at NIH approved a list of 31 priority research recommendations specific to Parkinson's that highlight areas in which NINDS and the broader field should direct its resources to achieve the greatest impact in addressing treatments and the underlying causes of the disease.[4] These recommendations were the result of an intensive planning process that brought together clinicians, researchers, and the patient community to determine the areas of greatest need to reframe how we approach the disease. We applaud NINDS for their leadership in this effort, which represents an unparalleled opportunity to coordinate critical initiatives to help unlock the mysteries of Parkinson's - but its success is dependent upon strengthening funding at NIH and NINDS to ensure that sufficient capacity and resources are available.

Unfortunately, due to ongoing fiscal constraints, including sequestration, the NIH research budget has not kept pace with inflation or the growing needs of an aging population and the overall public health. Sequestration alone cut over $1.55 billion from NIH in FY 2013, which is roughly equivalent to the entire budget for NINDS. NIH, the largest funder of Parkinson's research in the world, was also forced to reduce its Parkinson's-related research from a high of $154 million in FY 2012 to $135 million in FY 2013, a 12 percent decrease. Across the country, many institutions have felt the burden of these cuts, receiving smaller grants or no grants at all. As NIH continues to find high-priority areas to fund in order to advance Parkinson's research, we should be increasing support and not applying cuts that could possibly delay years of progress toward a cure for Parkinson's and other diseases.

In addition to the leadership of the NIH, the Department of Defense (DoD) funds Parkinson's research at the U.S. Army's Neurotoxin Exposure Treatment Parkinson's Research (NETPR) program. Started in 1997, the NETPR program has funded over $370 million in research grants to researchers across the country to support forward-looking research to better understand the wide range of toxins and other events, such as traumatic brain injury, that may lead to the onset of Parkinson's disease. Understanding how these exposures occur, the incidence of disease afterwards, and how these conditions may be prevented, treated, or cured will allow the DoD to better protect military personnel while they serve our country. Research findings can also be applied to the nearly 80,000 veterans living with Parkinson's disease. Among other things, the Parkinson's research program has supported development of compounds to treat conditions often associated with Parkinson's disease, such as depression, anxiety disorders, executive function disorders, and sleep dysfunction; investigations into specific links between environmental exposures and risk factors for Parkinson's disease; and research to understand the role of exercise to slow or delay progression of Parkinson's.

Recommendations for the 21st Century Cures Initiative

- ***Analyze Need for Additional Incentives.*** For our public health system, it will be imperative in the future to find better solutions to diseases like Parkinson's and Alzheimer's. We ask Congress to look at ways to encourage industry, venture capitalists, and others to invest in complicated, unmet medical needs, such as CNS diseases and disorders, through the use of creative tax laws, patent system reforms, exclusivity provisions, or other

[3] "An Economic Model of Parkinson's Disease: Implications for Slowing Progression in the United States," *Movement Disorders*, Vol. 28, No. 3, 19-26. 2013.

[4] "Parkinson's Disease 2014: Advancing Research, Improving Lives Final Recommendations," National Institute of Neurological Disorders and Stroke, 2014, https://meetings.ninds.nih.gov/assets/PD2014/NINDS_PD2014_Final_Research_Recommendations.pdf.

system reforms. If there is good science to pursue on Parkinson's, we want to ensure it is still not benched because of greater cost and less likelihood of success.

- ***Federal Funding for Research.*** Congress must increase investment in biomedical research in order to spur the development of future treatments and cures. In particular, we ask Congress to support the implementation of the 31 Parkinson's recommendations released by NINDS in January 2014 by increasing funding for NINDS and fully fund the Brain Research Through Advancing Innovative Neurotechnologies (BRAIN) Initiative, which aims to better understand the human brain through new technologies, tools, and mapping of the neuronal circuits.
- ***Research Reproducibility & Data Access.*** The issue of research reproducibility and access to unpublished data is one of great concern to patients who are relying on the forward progress of science for their disease. NIH Director, Dr. Francis Collins, and NIH Principal Deputy Director, Dr. Lawrence Tabak, have published recently on the steps NIH is taking to alleviate these problems.[5] We are encouraged by the new pilot training program, pilot program for evaluation of grant applications, and outreach to the research community being completed by NIH but ask Congress to watch the progress of these new NIH initiatives, many of which will be completed by the end of 2014, in order to increase efficiency and transparency of NIH-funded research. In addition, we encourage NIH and Congress to think about enforcement mechanisms that can be used to enforce publishing of data from NIH supported research.
- ***Pursue Designation of a Centralized Institutional Review Board (IRB) for Multi-Site Trials.*** A shift to a centralized IRB system would increase the efficiency of multi-site clinical trials. For individuals with Parkinson's, time is very much of the essence and an attempt to shorten the time-to-market for any promising treatment, prevention, or cure, while maintaining participant protections is strongly encouraged and welcomed. We encourage Congress to study the current IRB system and encourage the FDA to create a single IRB system.
- ***Use of Adaptive Clinical Trials.*** The FDA should be more accepting of sponsors' use of adaptive clinical trial design, which can increase the efficiency and the likelihood of success by allowing modifications in response to information learned in the course of the trial. We have heard that the Agency routinely permits only one adaptation in a trial, and that adaptation must be one that the sponsor anticipated and incorporated into the original trial design. The FDA should allow, when warranted by emerging data and in the best interests of trial participants and efficiency, for more than one adaptation.
- ***Encourage Use of Alternative Outcome Measures.*** There is no validated biomarker for Parkinson's. Because of this, current clinical trial design for Parkinson's disease treatments requires large samples, long durations of study, and great expense. We support the FDA's increased acceptance and encouraged use of surrogate endpoints and outcome measures, including patient-reported outcomes, and would like to see both NIH and FDA help industry create new outcomes measures for use in clinical trials.
- ***Become More Actively Involved in Ongoing Biomarker Initiatives.*** We encourage the FDA to become more engaged in projects such as the NINDS Parkinson's Disease Biomarker Project and the Michael J. Fox Foundation's Parkinson's Progression Markers Initiative (PPMI) to identify Parkinson's disease biomarkers. Groundbreaking initiatives such as these only stand to benefit from active FDA involvement. In addition, we encourage Congress to review the current biomarker qualification program at FDA and assess whether a new approach might be more useful to industry and science.
- ***Encourage Enhanced Communication to Build Awareness about Clinical Trials.***
  One contributing factor to the slow drug-approval rate for Parkinson's disease is the community's low clinical trial participation rate. At least seventy-one percent of people with Parkinson's report they are unaware of available clinical trials in their area. The NIH and FDA should encourage participation in clinical trials in a clear and concise manner through education and outreach, innovative recruitment techniques, and expanded reimbursement of trial expenses.
- ***Develop Guidance on Risk-Benefit Engagement.*** PAN was pleased that the *Food and Drug Administration Safety and Innovation Act* included provisions for FDA to look at how different disease populations look at risk-benefit. Our major concern with the current Patient Focused Drug Development Program is the series of twenty meetings and what this ultimately means for risk-benefit decision making. Parkinson's was selected as one of the 20 meetings along with Huntington's Disease, and we welcome the opportunity to educate the FDA on our disease, but want to better understand how the information gathered at the meetings will be used by the

[5] "Policy: NIH plans to enhance reproducibility," *Nature,* 505, 612–613 (30 January 2014), http://www.nature.com/news/policy-nih-plans-to-enhance-reproducibility-1.14586.

review division when a new drug application reaches their desks for review and how this information can be available much earlier in the drug development process. We encourage the FDA to draft a guidance on how and when industry can engage with patients to collect benefit-risk information and what type of data will be accepted by the Agency. Ultimately, this information could inform clinical targets, trial design, and new patient reported outcome measures.

Conclusion

Thank you for the opportunity to engage in this exciting initiative. We look forward to working with you and the Energy and Commerce Committee. For questions regarding Parkinson's disease or our recommendations, please contact Jennifer Sheridan, PAN director of policy, at [redacted]

Sincerely,

[redacted]

Amy Comstock Rick

PAN is the unified voice of the Parkinson's community advocating for better treatments and a cure. In partnership with other Parkinson's organizations and our powerful grassroots network, we educate the public and government leaders on better policies for research and an improved quality of life for the estimated 500,000 to 1.5 million Americans living with Parkinson's disease, for whom there is no treatment available that slows, reverses, or prevents progression.

PEAC
PATIENTS EQUAL ACCESS COALITION

June 13, 2014

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

The Honorable Diana DeGette
Member
House Energy and Commerce Committee
2125 Rayburn House Office Building
Washington, DC 20515

Sent via e-mail: Cures@house.mail.gov

Re: Request for Information (RFI) Regarding the 21st Century Cures Initiative

Dear Chairman Upton and Representative DeGette:

The Patients Equal Access Coalition (PEAC) appreciates the opportunity to submit these comments in response to the request for information from the patient community as part of the Committee's 21st Century Cures Initiative. PEAC is a patient-focused coalition which works to ensure that cancer patients have appropriate access to all approved anti-cancer regimens including, but not limited to, oral and intravenous drugs, intramuscular injections, surgery, radiation, and transplantation.

Patient access to self-administered anticancer therapies:

One of the most important and straight-forward things that the Committee can do to support innovation and reduce suffering for cancer patients is to ensure that patients have access to innovative therapies once they are approved.

Cancer patients face a barrier since insurance coverage has not kept pace with innovation in medicine and the growing trend towards orally and other patient-administered chemotherapy. Today, patient-administered chemotherapy has become more prevalent and is the standard of care for many types of cancer. Oral chemotherapy also accounts for approximately 35% of the oncology development pipeline. More importantly, many oral anti-cancer medications do not have intravenous (IV) or injected alternatives and are the only option for some cancer patients.

As these medications become more prevalent in cancer treatment, they must be as affordable as their IV counterparts. Traditionally, IV and injected treatments were the primary methods of chemotherapy delivery, which are covered under a health plan's medical benefit where the patient is only required to pay a small office visit co-pay. Since patient-administered anti-cancer medications are often covered under a health plan's prescription benefit, many patients are responsible for extremely high and unmanageable co-pays as high as hundreds or thousands of dollars per month. As a result, almost 10% of patients choose not to fill their initial prescriptions for oral anti-cancer medications due to the high rates of cost-sharing.[1]

To address this patient access challenge, PEAC supports H.R. 1801, the Cancer Drug Coverage Parity Act, which requires any private health plan that provides coverage for cancer chemotherapy treatment to provide coverage for self-administered anticancer medication at a cost no less favorable than the cost of IV, port

[1] Streeter SB, Schwartzberg L, Husain N, and Johnsrud M, Patient and Plan Characteristics Affecting Abandonment of Oral Oncolytic Prescriptions. Journal of Oncology Practice. Vol. 7, Issue 3S: 46s-51s, 2011.

administered, or injected anticancer medications. This law is not a mandate as it only applies to health plans that already cover chemotherapy. This bill ensures equality of access and insurance coverage for ALL anti-cancer regimens. Health insurance cost-sharing schemes should not create barriers to cancer patients' ability to access potentially life-saving medicines.

Coverage for Participation in Research at National Cancer Institute (NCI) Designated Cancer Centers:

An additional challenge is that a growing number of health insurance plans are excluding NCI-designated cancer centers from their networks, which impedes patient access to clinical trials.

Currently, there are 68 NCI designated cancer centers in the United States dedicated to the research and development of new technologies to prevent, diagnose, and treat all types of cancer. To earn this designation, these centers must meet rigorous criteria in multidisciplinary cancer research. According to a report prepared by Milliman, Inc. and commissioned by the Leukemia & Lymphoma Society (a PEAC member), many of the health plans that are participating in the insurance exchanges offer limited access to these NCI-designated cancer centers as they are not considered to be in-network.[2]

The Affordable Care Act's expansion in coverage of care associated with participation in clinical research will lead to better recruitment and access to alternative treatment options when patients exhaust already approved therapies. With much of this research occurring at NCI-designated cancer centers, PEAC is concerned that many plans do not consider these state of the art centers to be in-network. For these reasons, PEAC hopes to work with the Committee to encourage the inclusion of NCI-designated cancer centers in exchange plans.

Access to Novel Therapies:

There has been much attention paid to the pricing of newly approved drugs, which can be a challenging and divisive topic. Our coalition is focused on patient access to treatment and ultimately seeks to evaluate all potential solutions to ensure that cancer patients have access to the treatments recommended by their physicians. PEAC hopes to continue a dialogue with our industry partners, insurers and Congress on how best to assure patient access to the newest treatments.

Thank you very much for the opportunity to submit these comments to the 21st Century Cures Initiative. If you have any questions or would like additional information, please contact Jennifer Leib at [redacted]

Sincerely,

AIM at Melanoma
Cancer Support Community
Fight Colorectal Cancer
FORCE: Facing Our Risk of Cancer Empowered
Hematology/Oncology Pharmacy Association
International Myeloma Foundation
National Brain Tumor Society
Ovarian Cancer National Alliance
Roswell Park Cancer Institute
Susan G. Komen

[2] http://www.lls.org/content/nationalcontent/pdf/ways/Milliman2014IndividualExchangePoliciesinFourStates_20140109.pdf

Tuberous Sclerosis Alliance | forty years CHANGING LIVES 1974 • 2014 LIVES

June 13, 2014

The Honorable Fred Upton, Chairman
U.S. House of Representatives
Committee on Energy and Commerce
2125 Rayburn House Office Building
Washington, DC 20515

Dear Chairman Upton,

Thank you for inviting input from the patient community on the 21st Century Cures Initiative, a bi-partisan effort within the House Committee on Energy and Commerce to impact the discovery, development, and delivery of new cures and treatments.

The Tuberous Sclerosis Alliance (TS Alliance) is dedicated to finding a cure for tuberous sclerosis complex (TSC) while improving the lives of those affected. TSC is a rare genetic disorder that causes non-malignant tumors to form in many different organs, primarily in the brain, eyes, heart, kidney, skin and lungs. The aspects of TSC that most strongly impact quality of life are generally associated with the brain: seizures, developmental delay, intellectual disability and autism. Because manifestations of TSC are related to many more prevalent disorders—autism, cancer, epilepsy, etc.—TSC is considered a "linchpin" disease. Research to better understand these aspects of TSC will give scientists insight into many related disorders, as well.

The TS Alliance catalyzes and sponsors TSC research, develops programs and resource information about the disorder, and implements public and professional educational programs designed to heighten awareness of TSC. Since 1984, the TS Alliance has funded $17.4 million in support of basic, translational and clinical research. Because of our advocacy for research and support of young investigators, we have cultivated a new generation of scientists who have received more than $198 million in competitive research awards from the National Institutes of Health (NIH) and the Department of Defense Congressionally Directed Medical Research program (CDMRP).

In response to 21st Century Cures' third white paper, entitled "21st Century Cures – Patients," the TS Alliance respectfully submits input to several of the questions posed to the patient community by the Committee on Energy and Commerce.

What is the state of discovery of cures and treatments for TSC?

There is no cure for TSC. Over the past two decades, research has led to identification of two genes that can cause TSC and to the finding that the genetic defect in TSC causes increased activity of mTOR, a protein in the cell that stimulates cell growth. It is this excess mTOR activity that leads to tumors in many organs. As a result, one drug that inhibits mTOR has been approved for the treatment of two types of tumors—brain and kidney—in TSC.

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However, this drug shrinks and stabilizes tumor growth, but it does not eliminate the tumors. When the drug is withdrawn, the tumors begin to grow again. Additionally, although researchers are hopeful that this drug may impact the neurological effects of TSC such as epilepsy and autism, this has yet to be proven.

Clinical studies are underway to identify biomarkers that will identify infants with TSC who are at risk of epilepsy and autism earlier than they can be identified now. But the best way to treat those infants, when identified, has yet to be discovered. Even if an effective, early treatment is found, it only addresses the complications of TSC—it is not a cure.

What programs or policies has the TS Alliance utilized to support and foster research, such as patient registries, public-private partnerships, and venture philanthropy?

Since 2006 the TS Alliance has operated a patient registry, the TSC Natural History Database. This project has collected clinical data on more than 1300 Americans affected by TSC of all ages, genders, and ethnic backgrounds. The course and severity of the disorder is highly variable among individuals—even among identical twins.

To enhance this database and increase its impact, the TS Alliance partnered with a pharmaceutical company that generously sponsored expansion and improvement of the registry. However, the data remain owned by the TS Alliance, and any researcher can access the data. This partnership is one in which everyone wins: the company has access to a more robust dataset, all researchers (even at other companies) also have access to the improved dataset, and the patients ultimately benefit from their data being used to develop improved treatments. We would welcome the opportunity to discuss the design and impact of this partnership with the committee.

How can Congress incentivize, coordinate, and accelerate basic research for diseases we know relatively little about?

Biomedical research is expensive, but a small amount of directed funding can have incredible ripple effects to incentivize research. The TS Alliance has demonstrated this, as recipients of our small grants, generally $66,000 per year or less, have gone on to obtain more than 10 times more funding from the NIH and CDMRP. Many researchers who have dedicated their careers to TSC received their first grant from the TS Alliance—another example of small, directed funding having long-lasting impact.

Congress should appropriate sufficient resources to the Office of Rare Diseases Research (ORDR) within NIH's National Center for Advancing Translational Science (NCATS) to coordinate and accelerate basic research on rare and poorly understood diseases. ORDR has been an outstanding partner to the TS Alliance and other rare disease-focused organizations. ORDR is ideally suited to coordinate basic research

on rare disorders across all NIH institutes and offices, and ORDR can facilitate translational work on rare diseases thanks to its positioning within NCATS.

How do you coordinate your research and outreach with other patients?

The TS Alliance works closely with organizations that fund research on disorders and projects related to TSC. As one example, the TS Alliance initiates a one-day Trans-NIH TSC meeting every one or two years. The Trans-NIH meeting consists of the TS Alliance, CDMRP Tuberous Sclerosis Complex Research Program officials, and program officers from all nine NIH institutes that fund research related to TSC. The TS Alliance contributes patient-focused points of view on the most impactful unmet medical needs for research. All attendees share the types of research grants and programs funded by each; this discussion ensures alignment of research emphasis and, simultaneously, lack of duplicative funding for essentially identical projects.

As another example, the TS Alliance has co-funded research projects with organizations that advocate for related disorders, including lymphangioleiomyomatosis (LAM) and polycystic kidney disease (PKD). The TS Alliance also communicates regularly with many other organizations, including those representing Birt-Hogg-Dubé Syndrome, Von Hippel-Lindau Disease, various specific types of epilepsy, and more.

What can we learn from your experiences with clinical trials and the drug development process?

The TS Alliance has been an early partner in the development of many clinical study protocols, whereas some other clinical studies were developed without patient input. Those developed with patient advocates as early partners were executed much more successfully because the priorities and concerns of patients were considered during study protocol design.

Regardless of whether we were involved at an early stage or not, the TS Alliance works to increase awareness of upcoming and ongoing clinical studies to encourage those with TSC who are eligible to consider participating. We know from clinical researchers that the TS Alliance's efforts have made a major impact on recruitment.

The TS Alliance helped catalyze the formation of a TSC Clinical Research Consortium in 2012 that began with five geographically distributed academic medical institutions with active TSC Clinics and research efforts. With the TS Alliance as a partner to make constituents aware of the studies, the consortium enrolled two multi-million dollar NIH-funded clinical studies ahead of schedule. This outcome is all the more impressive when one realizes that both clinical studies were enrolling newly diagnosed infants—not recruiting from a well-connected, long-standing population.

We are convinced that these successful clinical studies result from utilizing a small number of focused study sites. A smaller number of investigators, sites, and

processes present fewer opportunities for variability. Other studies in TSC that have attempted to cast a wide net by using a large number of sites have actually been less successful at recruitment due to lack of focus. We recommend the committee utilize a small number of focused clinical research centers to have the best chance of successfully impacting clinical research in rare disorders.

How should regulators evaluate benefit-risk? How do you work with regulators regarding benefit-risk? Can this process be improved?

In short, regulators can best evaluate benefit, and patients or their family members can best evaluate the risk they are willing to accept. Only an open, detailed conversation between regulators and patient advocates can produce a reasonable evaluation of benefit-risk.

After the conclusion of clinical trials, the TS Alliance has been involved in discussions with the FDA for the approval of vigabatrin for infantile spasms and of everolimus for a certain type of brain tumor associated with TSC. Both of these drugs, for very different reasons, were considered to have serious risks. However, parents of the target population (both approvals were for pediatric indications) were able to articulate their willingness to accept certain levels of known and unknown risk because of the very clear risk to their children in the absence of those drugs.

Congress, regulators, and healthcare providers must realize that the principle of "first, do no harm" must be viewed from the patient's perspective—in many cases, particularly with progressive rare disorders, *doing nothing is clearly doing harm*.

Even after a new treatment is approved by regulators, excessive requirements to protect against very rare—and sometimes theoretical—risks can impose a major barrier to access. REMS (Risk Evaluation and Mitigation Strategies) should be used sparingly, because they impose a burden of time upon patients and caregivers, discourage appropriate use by eliciting fear, and increase costs. The TSC community has observed this with the severe REMS restrictions on vigabatrin, a drug that is effective at treating infantile spasms (a severe type of epilepsy) in 90 percent of infants with TSC—when doctors and caregivers are not afraid to try the drug. Again, patients and caregivers are often willing to accept risk when the outcomes without treatment are devastating, but severe REMS restrictions can be out of proportion to clinically documented risk vs. clinically documented benefit.

What is the role of public and private funding in the research and development of cures and treatments?

Private funding is ideal for the early stages of basic, discovery research and for the late stage of product development. In the former case, private funding from disease-specific groups such as the TS Alliance catalyzes work on the specific disorder of interest. This type of funding encourages work in a disease area that might not otherwise be attractive to an investigator. It encourages new, radical ideas because

the disease-focused groups, which are generally patient-driven groups, are highly motivated to generate new directions for research and to recruit new investigators to their ranks. In the latter case, private funding (usually pharma or venture capital) will invest in a late-stage project when the prospect of a financial return is worth the risk.

Public funding is critical when the immediate financial payoff is not likely or not obvious. This includes basic research into new biology or new technology. It includes the development of disease models. In the case of rare disorders, which are a high financial risk for private investors, public funding is critical for the types of translational and clinical work that NCATS can support.

Are there success stories the committee can highlight and best practices we can leverage in other areas?

We recommend three success stories outlined above:

1. Partnership between the TS Alliance and pharma to fund enhancements in a patient registry that remains owned by the TS Alliance and available to all researchers.
2. The TSC Clinical Research Consortium that focuses a small number of expert centers on a small number of clinical projects in partnership with the TS Alliance to ensure successful recruitment of study participants.
3. Open communication with funders of disease-specific research, in our case the TS Alliance, CDMRP, and nine NIH institutes and offices.

How can Congress help?

The purchasing power of NIH funding has dropped dramatically over the last few years. Congress must restore research funding to 2003 levels relative to inflation and maintain it. The cost of research is largely driven by personnel, which means that research funding, by definition, creates jobs. The intellectual work of personnel cannot be miniaturized or relegated to robots, so the cost of research will continue to increase with the cost of living. Public research funding must increase in parallel with the cost of living just to maintain existing levels of research productivity.

Regulatory policy and public research funding must remain consistent over the long period of time required to turn basic research into a new treatment. Assuming that the development of a new drug takes roughly ten years, disruptive changes in policy and funding at a rate greater than every ten years creates a moving target that no one can hit. Stable policy and funding expectations are required to enable researchers to move projects from idea to impact.

Congress can require regulations to keep pace with the realities of modern science. A specific example is the concept of the Institutional Review Board (IRB). The need for protection of human subjects is as strong as ever. However, the three TSC success stories listed in the preceding section are all dependent upon partnership, collaboration, and consortia. IRBs administered by individual institutions are archaic

and a major impediment to collaborative research. Congress must instruct regulators to provide for review boards that ensure protection of human subjects on a nationwide scale, not at the level of a single institution. This single policy change would have a major impact on the speed of initiating collaborative clinical studies as well as a significant cost savings.

In conclusion, thank you for the foresight and courage to lead this bi-partisan effort to improve biomedical research and healthcare for all Americans. We appreciate the opportunity to comment, and the TS Alliance stands ready to help the committee in any way we can to advance 21st Century Cures for the benefit of all patients.

Sincerely yours,

[redacted]

Kari Luther Rosbeck
President and CEO

[redacted]

Steven L. Roberds, Ph.D.
Chief Scientific Officer

[redacted]

Debora Mortiz
Government Relations
Committee Chair

USAgainstAlzheimer's
we can stop it by 2020.

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VIA ELECTRONIC DELIVERY

June 13, 2014

Committee on Energy and Commerce
2125 Rayburn House Office Building
Washington DC 20515

Re: 21st Century Cures Initiative

Dear Chairman Upton, Representative DeGette and Members of the Committee:

Thank you for undertaking the 21st Century Cures Initiative. As both of you have noted in introducing the initiative, this comprehensive, bipartisan look at the multiple components of our research and development infrastructure – public and private – is urgently needed. Today, Congress has an opportunity to develop thoughtful policy changes that will serve human health and well-being and slow the growth in our entitlement costs for the benefit of generations to come.

As you look to gain a better understanding of these issues from the patient community, I encourage you to prioritize your efforts around areas of greatest need. While your intent is to shy away from disease specific considerations, and this is understandable, there is one disease that stands apart and calls for special focus and consideration as a model of how a 21st Century cures system can address massive unmet needs: Alzheimer's disease and dementia.

Alzheimer's presents a national crisis. There is no disease modifying treatment available today despite the billions of dollars invested by industry and multiple, late-stage drug failures. This course of failed drug development must be understood and addressed if we are to avert the looming health and financial burdens of this devastating disease.

There is, however, hope. Innovations are emerging that warrant examination by this Committee. These innovations are aligning forces – public and private, domestic and global – in unprecedented ways to fight this disease, providing potential models for new means of addressing the most daunting health challenges of our time. Changes in policy can dramatically change the risk/reward balance and encourage greater private investment in Alzheimer's drug development. The collaborative platforms that are unfolding present new blue prints for the way government and the private sector must work together to change human health. Our policy architecture, including agency funding priorities and authorities, must be designed to serve these new models for collaboration and this is an appropriate task for your Committee.

I strongly urge you to elevate Alzheimer's disease within the 21st Century Cures Initiative as a model application, given both the immense impact of the disease on our health and financial well-being and because of the opportunity to examine in the context of this looming crisis the kind of emerging public private collaborations that will be essential for government to leverage its precious resources and meet the challenges of the 21st Century.

The following answers provide insights into the unique work taking place in both the public and private sectors to advance our understanding of Alzheimer's disease. We look forward to working with you to consider a focused roundtable on policy strategies to support this critical work.

1. **What is the state of discovery of cures and treatments for your disease? Are there cures and treatments now or on the horizon?**

Few diseases or disorders underscore the urgent need for the expeditious development of safe and effective therapies than Alzheimer's disease and related dementias. More than 5 million people in the United States are estimated to be dying with Alzheimer's disease today, and a study out earlier this year indicates that more than 500,000 deaths each year are attributable to Alzheimer's, making the disease our third leading cause of death. We have no disease modifying treatments or means of prevention available today, making Alzheimer's the only leading disease where patients and family members have no hope the disease can be modified, slowed or lessened today. This lack of hope exacerbates the need to focus on Alzheimer's in the 21st Century Cures Initiative.

2. **What programs or policies have you utilized to support and foster research, such as patient registries, public-private partnerships, and venture philanthropy?**

In 2012 the Administration, supported by the Advisory Council on Alzheimer's Research, Care and Services, set as its first goal the prevention and effective treatment of Alzheimer's disease by 2025. This step was viewed as bold, warranted, and historic for government. The goal and the commitment required to meet it was embraced across sectors, but it was widely accepted that that government, acting alone, would not be able to meet the 2025 objective. Still, there existed no formal platform by which industry and non-profit leadership could convene to become this working partner with government.

To address this need, **The Global CEO Initiative on Alzheimer's Disease (CEOi)** was formed. This is a groundbreaking industry-NGO coalition committed to work with governments in the US and abroad in public-private partnership in order to achieve the US goal – subsequently embraced in December 2013 by the G8 – of finding a means of prevention and effective treatment of Alzheimer's by 2025.

The CEOi, composed of the leaders of a dozen major corporations across multiple sectors, [1] is engaging in this fight with vigor, aligning the competencies and shared resources of government, industry and nonprofit sectors. This collaboration will deliver an action-oriented, results-driven approach to increasing the prospect of achieving the global 2025 goal.

Recommendation: Innovations in the Alzheimer's community are worthy of study by the Committee with specific focus on what policy changes might take place to assure that private

[1] AC Immune, Bank of America, Banner Health, GE, Home Instead Senior Care, Janssen, Lilly, Merck, Nestle Health Science, Pfizer, Sanofi, and Takeda.

investment is incented to drive innovation in the discovery and treatment of Alzheimer's. The CEOi is well-positioned, given its corporate representation from Japan to the US to Europe and the breadth of its work here and abroad, to provide insight in this work.

3. How can Congress incentivize, coordinate, and accelerate basic research for diseases we know relatively little about?

For millions of American's living with Alzheimer's and their families, we are thankful that Congress and the Administration have recognized the threat of Alzheimer's and the need for meaningful action right now. In 2011, the National Alzheimer's Project Act (NAPA), which required the United States to establish a strategy to address the disease, was enacted into law following unanimous Congressional approval. In 2012, the National Plan to Address Alzheimer's was released with goal 1 being preventing and treating the disease by 2025. Considering the scientific landscape, including a slew of late-stage failed trials, this is a bold yet necessary time-bound goal, one the nation must pursue with the same gusto it mustered when setting out to win the space race, map the human genome or make inroads against other diseases like cancer, heart disease and HIV/AIDS.

Congress and the Administration have both acted in recent years to increase the amount of funding available for research into Alzheimer's disease at the NIH. While welcome, particularly during the age of tight budgets and sequestration, the reality is that today the U.S. commits about $560 million in NIH funding to Alzheimer's disease. This represents only about ¼ of the amount of public research funding leading experts think is needed to maximize our likelihood of achieving the 2025 goal.

We have been fortunate that concurrent with our efforts in the United States, other global nations have recognized the threat of Alzheimer's and dementia, have enacted national plans or strategies of their own and, to some extent, have called for or allocated additional resources to dementia research. Late last year, Prime Minister David Cameron convened the landmark G8 (now G7) Dementia Summit in London. The group issued a declaration endorsing a goal quite similar to the U.S.'s 2025 goal and also supporting the commitment of additional resources to the cause. This year, the G7 will convene a number of legacy workshops, with the final session, focused on the global Alzheimer's research strategy, set to be held at the NIH in February 2015. Just recently, the effort created the World Dementia Council, which is intended to drive the G7 work going forward.

The UK Legacy event focused on increasing global resources will focus on the policy, regulatory, industry practice and financial model innovations needed to increase private investment in Alzheimer's discovery, development and care. While increases in public resources are necessary to invest in basic and translational science, private investment in drug development must also be encouraged through changes in policy and regulation that will increase the rewards and reduce the risk of seeking a cure or treatment for Alzheimer's.

Recommendation: Congress's commitment through the NAPA process has created a solid platform for moving the field forward. Today, this Committee is positioned to build upon this platform and consider, with input from the community, policies to support and accelerate drug development in Alzheimer's. Areas that should be reviewed are:

- **Consideration of legislation to provide market exclusivity – independent of patent life – for compounds that attenuate Alzheimer's pathology and slow dementia progression. See testimony of Kenneth L. Davis, June 10, 2014.**[2]
- **Call for, and recommend funding for, a standing, trial-ready global clinical trial network (see discussion below) that would:**
  - **Be a public private partnership endeavor;**
  - **Integrate global registries of patients who will become qualified for participation in clinical trials and who can be followed longitudinally to provide key insights into prevention, healthy aging, interactions of genes and environment in the onset of Alzheimer's, as examples; and**
  - **Align forces with similar efforts abroad to bridge geographical boundaries to assure optimal efficiencies, knowledge sharing and accelerate discovery.**
- **Examine with the FDA policy changes that will provide access to trial data from failed trials in a manner that will not interfere with future potential development but will assure that the knowledge gained from human contributions to research becomes generalizable and available to spur discovery and avoid unneeded, wasteful replication.**
- **Ensure robust implementation of the Food and Drug Administration Safety and Innovation Act (FDASIA) provisions intended to accelerate the FDA review process to ensure future Alzheimer's applications will receive the swiftest review possible.**

4. How can we work together to better translate advances in science into safe and effective new therapies for patients?

See above.

5. What can we learn from your experiences with clinical trials and the drug development process?

The Global CEO Initiative on Alzheimer's Disease – a coalition convened by USAgainstAlzheimer's, a nonprofit patient advocacy organization – has joined with the New York Academy of Sciences to co-lead an effort to develop the **Global Alzheimer's Platform (GAP).** This initiative represents another innovation that is emerging that deserves to be highlighted and understood as part of the Committee's work.

The Global Alzheimer's Platform, or GAP, aims to install a more efficient clinical translational infrastructure with greater data sharing and transparency. Built on a precompetitive clinical trial approach that shares resources and reduces duplicative efforts GAP will facilitate approaches that "fail fast and learn quickly." Supported by a new public-private partnership, GAP aims also to build a framework for greater cooperation and data sharing between existing and future Alzheimer's disease drug development efforts.

[2] Testimony, Kenneth L. Davis, M.D., Chief Executive Officer and President , Mount Sinai Health System Energy and Commerce Committee, Subcommittee on Health, "21st Century Cures: Examining the Role of Incentives in Advancing Treatments and Cures for Patients", June 11, 2014.

To meet these objectives, GAP is designed to:

1. Establish a global system of standardized and linked registries and cohorts from which investigators can contact well characterized trial-ready participants;
2. Stand up a global network of clinical trial sites that employ standardized protocols and datasets and are certified for quality, efficiency, and performance; this network would be linked to the registries/cohorts to facilitate speedy recruitment of the right subjects;
3. Develop flexible and innovative clinical trial designs that enable adaptive and combination trials; and facilitate moving from learning to confirmatory trials; and
4. Develop financing mechanisms to sustain the installation and maintenance of a standing global AD platform.

Work streams to accomplish each of the objectives outlined above are co-led by a member of industry and a leading academic researcher in Alzheimer's disease. To assure the highest level of performance and project management, industry partners are providing the leadership through a small set of "Executives on Loan". By creating a platform that addresses both access to a trial-ready set of well characterized patients as well as a global network of qualified sites that can run both 'learn' and 'confirm' trials in a spectrum of AD subjects with multiple treatment arms, GAP would both increase the speed, quality and probability of success for new and emerging treatment approaches in AD, with reduced risk of Phase 3 failure. It is the goal of GAP to gain about 24 months of development time with about a 20% reduction in overall number of subjects needed. With more effective learning also probability of success of assets graduating to confirmatory trials will be significantly higher than current benchmarks. Coordination with similar efforts around the world, including the work of the Innovative Medicine's Initiative in Europe, will be a core feature as well.

Significantly, the FDA has met with the leadership of GAP and has committed talent from the agency to serve as a liaison to the initiative. We commend the FDA for this willingness to collaborate, assure that goals for GAP are aligned with both private and public sector needs, and operate with commendable transparency.

Recommendation: The GAP initiative stands ready to be examined by the Committee through a process where the leadership of GAP can provide input on legislative mechanisms needed to assure that the FDA and NIH have the authorities, resources, and latitude to participate in a groundbreaking global public private endeavor of this critical nature.

6. What is the role of government in your work, including any barriers to achieving your goals and advancing breakthroughs?

The Global CEO Initiative on Alzheimer's Disease (CEOi) is a groundbreaking industry-NGO coalition committed to work with governments in the US and abroad in public-private partnership in order to achieve the G8 and US goal of finding a means of prevention and effective treatment of Alzheimer's by 2025. As discussed in Section 2 above, the CEOi, composed of the leaders of major corporations across multiple sectors, was formed in response to the invitation to industry by governments to join in the

global fight-back against Alzheimer's. Members of the CEOi are engaging in this fight with vigor, but recognize its goals cannot be achieved without innovative public-private partnerships that align the competencies and shared resources of government, industry and nonprofit sectors. This collaboration will deliver an action-oriented, results-driven approach to increasing the prospect of achieving the global 2025 goal.

In particular, the CEOi is working with the National Institute on Aging (NIA) to host an off-year research summit that is complementary to the Alzheimer's Research Summit that will be held by the National Institute on Aging at the NIH every two years. The CEOi-led research summit, co-sponsored in collaboration with the NIA, stands as an opportunity for industry to provide discrete input in the nation's Alzheimer's research agenda.

Recommendation: We are not aware of any similar effort where government and industry, with aligned missions and purposes to tackle a global health problem, have structured a complementary process to align policy changes and industry practice innovations to accelerate a critical national health and economic goal. This complementary and coordinated model can be replicated across disease states and should be examined by the Committee.

7. What is the role of public and private funding in the research and development of cures and treatments?

See comment above, Section 5, regarding the Global Alzheimer's Platform (GAP).

8. Are there success stories the committee can highlight and best practices we can leverage in other areas?

Yes. Given the robust level of public-private collaboration and global approach – as described in the previous section, I would urge you to consider examining the work of the Global CEOi and its various initiatives, including GAP, as new, informative innovations that have the potential to play a critical role in our nation's response to the Alzheimer's crisis.

Recommendation: A roundtable should be convened that will focus on game-changing global collaborations and/or public-private partnerships that are emerging to address daunting diseases, including Alzheimer's, and the new understandings of the essential need for government to work in new ways with the private sector to execute on coordinated mechanisms of change in policy and industry practice to achieve a public health goal. GAP, for example, could very well become a model that can be followed for efforts to advance therapy development for an untold number of conditions and diseases. Its leadership is ready to discuss this prospect with the Committee.

9. What is the financial burden of your disease? How would better treatments and cures help save money for your family and the federal government?

In addition to being a major threat to our health, Alzheimer's also poses a significant threat to our economy in both the public and private sector. Research by the RAND Corporation last year found that

direct costs of Alzheimer's disease and dementia exceed those of cancer and heart disease and that total costs, including caregiving, could exceed $200 billion each year. About 70 percent of these costs are shouldered by the taxpayers through Medicare and Medicaid expenditures. As daunting as this may be, it is nothing compared to the estimated $1 trillion annual price tag of the disease by mid-century if the current trajectory remains as is.

Development and approval of disease-modifying therapies and treatments could significantly lessen the cost impact on government and families. For example, even if a treatment is only able to modify or delay the disability symptoms of the disease by 3 to 5 years, the nation would achieve significant public savings in terms of reduced care costs, particularly less costs associated with institutional care. Late last year, the consulting group RTI published a paper stating that if appropriate changes are made to our drug development system to remove barriers, such changes could reduce development costs of a single Alzheimer's therapy from about $5.7 billion to about $2 billion and shorten the timeframe by about 16 months. Perhaps most exciting, were this pace to be accelerated, the report predicts avoidance of about 7 million cases of Alzheimer's during a 15 year period between 2025 to 2040.[3]

New financing models that combine large-scale private investment and government guarantees hold the promise that major new global finance streams can be brought to bear on Alzheimer's outside the traditional NIH and other national funding mechanisms. Innovative finance mechanisms not reliant on annual government appropriations but on global capital markets offer an opportunity to utilize global concerns about Alzheimer's to finance major leaps forward in research and drug development.

10. How can Congress help?

Recommendation: I would also urge you to strongly consider the following policy issues in a potential 21st Century Cures legislative package:

- **Bolster funding for the NIH, including a multi-year process to restore the purchasing power lost over years of flat or declining budgets.**
- **Implement a more effective and transparent process for establishing, reviewing and revising the funding priorities of the NIH, one that seeks to ensure scarce resources are matched against the greatest burdens and opportunities.**
- **Provide the clearest direction possible to the FDA that any Alzheimer's therapy – whether disease-modifying or one able to slow the advent of disability symptoms – be eligible for the swiftest review possible.**
- **Establish a process to facilitate the global sharing of data (including from clinical trials and other sources) to assure that vital knowledge gained from human research participation is disseminated and unnecessary duplication of time and cost of potentially futile drug development efforts is avoided.**

[3] "Economic Analysis of Opportunities to Accelerate Alzheimer's Research and Development," RTI International, 2013.

- **Assure that FDA and NIH have sufficient authorities, resources and Congressional support to become vibrant and critical partners in new public private initiatives such as the CEOi and GAP.**

- **Consider the importance in an increasingly globalized environment for regulatory harmonization to optimize data standardization, global efficiencies in regulatory review, and data sharing, without compromising the values of safety and efficacy that guide FDA review.**

- **Consider innovative financing mechanisms that foster increased private financial and philanthropic investments with government serving as a credit enhancement or minority investor.**

Thank you for your leadership on this important initiative. If you have any questions, please feel free to contact me or reach out to Nick Manetto with USAgainstAlzheimer's at [redacted]

[redacted]

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