Memorial Sloan-Kettering
Cancer Center

Richard J. O'Reilly, M.D.

Chairman, Department of Pediatrics
Chief, Bone Marrow Transplantation Service
Claire L. Tow Chair in Pediatric Oncology Research

April 24, 2015

The Honorable Frank Pallone
Ranking Member, Committee on Energy and Commerce
United States House of Representatives
2125 Rayburn House Office Building
Washington, D.C. 20515

Dear Representative Pallone:

I am writing on behalf of Memorial Sloan Kettering Cancer Center (MSKCC), the oldest hospital in the nation devoted solely to the research and treatment of cancer, to ask for your support to improve children's access to cancer drugs by including the provisions championed in the Kids' Innovative Drugs (KIDS) Initiative as part of 21st Century Cures.

At Memorial Sloan Kettering, we care for children with all types of cancers, from the most common to the rarest, and at any stage, including a cancer recurrence. Our patients receive the latest, most-effective cancer treatments, and in some cases have access to innovative therapies through clinical trials, many of which may not be available elsewhere. However, children's access to cancer drug therapies often lags significantly behind adults' access, and changes are needed to improve the speed at which these drugs are made available to pediatric patients.

The reforms championed by the KIDS Initiative would address these challenges by amending the Pediatric Research Equity Act (PREA) to pilot an extended application of PREA to cancer drugs with a molecular target that is highly relevant to pediatric cancer. It would also reform the Best Practices for Pharmaceuticals Act (BPCA) to include a pilot applying only to cancer drugs, which would extend additional exclusivity when certain pediatric study requirements are met. We urge you to include these promising approaches to expanding treatment options for children with cancer as part of 21st Century Cures.

We greatly appreciate your leadership on issues of importance to the health care community as the 21st Century Cures Initiative takes shape. We hope you will extend your support to the KIDS Initiative. If you have any questions or we can be a resource to you as you continue your efforts, please contact Julie Belelieu at 646.227.2788.

Sincerely,

Richard J. O'Reilly, MD
Chair, Department of Pediatrics
Chief, Pediatric Bone Marrow Transplant Service
Claire L. Tow Chair in Pediatric Oncology Research

cc: Paul Nelson
Senior Vice President, Financial Planning

Nancy Goodman
Executive Director, Kids v Cancer

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Muscular Dystrophy Association
mda.org

May 19, 2015

The Honorable Fred Upton
Chairman, Committee on Energy & Commerce
U.S. House of Representatives
Washington, DC 20515

The Honorable Joe Pitts
Chairman
Committee on Energy & Commerce
Subcommittee on Health
U.S. House of Representatives
Washington, DC 20515

The Honorable Diana DeGette
Committee on Energy & Commerce
U.S. House of Representatives
Washington, DC 20515

The Honorable Frank Pallone
Ranking Member
Committee on Energy & Commerce
U.S. House of Representatives
Washington, DC 20515

The Honorable Gene Green
Ranking Member
Committee on Energy & Commerce
Subcommittee on Health
U.S. House of Representatives
Washington, DC 20515

Dear Chairmen Upton and Pitts and Ranking Members Pallone, Green, and DeGette:

On behalf of the thousands of families and individuals we serve, the Muscular Dystrophy Association (MDA) appreciates your leadership and commitment to 21st Century Cures Act. We see many opportunities and face great challenges—we commend the Energy & Commerce Committee for setting forth a collaborative structure in the 21st Century Cures Act in which government, individuals and industry work together to accelerate the discovery, development and delivery of cures to patients.

MDA is the leading nonprofit health agency dedicated to saving and improving the lives of people affected by neuromuscular diseases including the muscular dystrophies, spinal muscular atrophy (SMA), amyotrophic lateral sclerosis (ALS), Friedreich's ataxia (FA) and others. Despite more than six decades of investments, collaborations and research progress, people living with neuromuscular diseases still are in urgent need of comprehensive treatments and cures. Infants diagnosed with spinal muscular atrophy

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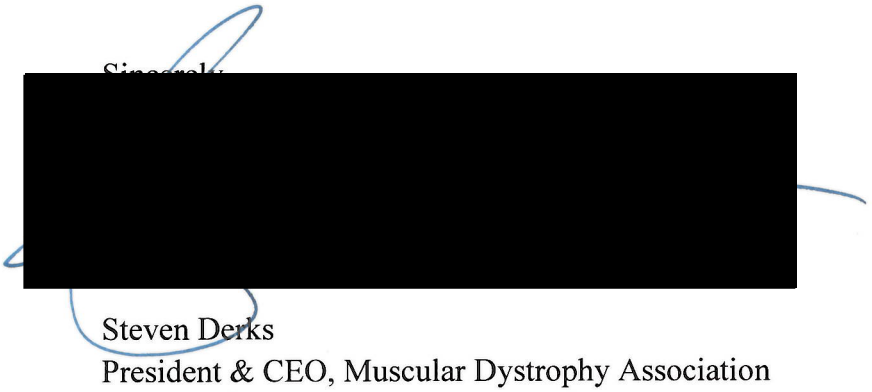
type I (SMA I) typically die before age two. Adults diagnosed with amyotrophic lateral sclerosis (ALS) typically die three to five years from the time of symptom onset. Those with Duchenne muscular dystrophy (DMD) have seen an improvement in their lifespan, as it is becoming more common to see individuals with DMD living into their 30s—but that lifespan is far too short.

We have seen first hand how public-private partnerships can spur dramatic advancements in understanding the mechanisms of and potential treatments for neuromuscular disease. To that end, MDA has awarded over $1 billion in research grants to propel the development of potential therapies since its inception. But the need for additional research can only be met with increased federal funding.

MDA applauds the Committee for increasing National Institutes of Health (NIH) funding set forth in the 21st Century Cures Act, which combined with the proposed NIH Innovation Fund, will help fuel the research that is necessary to save and improve the lives of those living with neuromuscular diseases. MDA appreciates the Committee's creativity and extraordinary efforts in pursuing this legislation.

Sincerely,



Steven Derks
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THE NATIONAL COALITION FOR CANCER RESEARCH

April 24, 2015

Member Organizations

American Association for Cancer Research

American Cancer Society Cancer Action Network

American Childhood Cancer Organization

American College of Radiology

American Society of Clinical Oncology

American Society of Hematology

Association of American Cancer Institutes

Coalition of Cancer Cooperative Groups

Friends of Cancer Research

International Cancer Advocacy Network

International Myeloma Foundation

Kidney Cancer Association

LUNGevity

The Lustgarten Foundation

Melanoma Research Alliance

Pancreatic Cancer Action Network PanCAN

Prevent Cancer Foundation

Prostate Cancer Foundation

The Society of Gynecologic Oncology

The V Foundation for Cancer Research

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www.cancercoalition.org

The Honorable Fred Upton, Chairman
Committee on Energy and Commerce
United States House of Representatives
Washington, D.C. 20515

The Honorable Diana DeGette
United States House of Representatives
Washington, D.C. 20500

Dear Chairman Upton and Representative DeGette:

The NCCR is a 501(c)(4) nonprofit companion advocacy organization of the National Coalition for Cancer Research. Comprised of 20 national cancer organizations, the mission of NCCR is to educate public policy makers, legislators and their staff about the impact of specific legislative initiatives on cancer research. Specifically, the NCCR advocates on behalf of legislation that will enhance and expand basic, translational and clinical research, and ensure that the infrastructure and reimbursement mechanisms are in place to support the translation of research from the laboratory to the bedside. The NCCR supports these goals in the broadest terms, emphasizing national priorities essential to progress in cancer research, education, treatment, early detection and prevention.

NCCR would like to express its sincere gratitude and support for your bipartisan leadership in the development of the 21st Century Cures initiative. We are especially appreciative of the open and inclusive process by which the proposal was developed, taking into account the recommendations and viewpoints of a wide variety of stakeholders. We strongly believe the goals and objectives outlined in the January 27, 2015 discussion document represent an innovative framework that will advance basic, clinical and translational biomedical research on cancer and many other diseases.

NCCR appreciates the opportunity to provide our comments and recommendations regarding the 21st Century Cures discussion document. Our comments are consistent with the mission of NCCR and our patients, and therefore focus on provisions of particular importance to the advancement of cancer research and treatment. We welcome the opportunity to continue to work with the Committee on this important legislation.

Increased Resources for NIH and FDA

The goals and objectives of the 21st Century Cures legislation are wide-ranging and innovative. We are concerned, however, that the proposal does not include a general authorization of additional appropriations to the National Institutes of Health or the US Food and Drug Administration. Without additional resources, achieving the laudable objectives included in the 21st Century Cures proposal could have the unintended consequence of diverting already scarce resources of these Agencies. For the 21st Century Cures to be successful, it must be funded through a new, higher baseline so that ongoing and future areas of scientific exploration on cancer and other diseases can continue and expand.

Surrogate Endpoint Qualification and Utilization (Sections 1021-1024)

The understanding and use of surrogate endpoints is increasingly becoming an important component of cancer research and the development of new cancer therapeutics. While overall survival remains the "gold standard" among endpoints for oncology, the use of surrogate endpoints provides many advantages to researchers and patients. Surrogate endpoints such as objective response rate, disease- and progression-free survival, and time-to-progression are being utilized successfully to more rapidly assess the effectiveness of new therapies in a shorter time span. The use of surrogate endpoints has reduced the time it takes to complete clinical trials, resulted in reduced FDA approval times, and has benefited patients by accelerating their access to new, and potentially life-saving, medicines, and allowing further data to be generated while agents are made available to patients at an earlier time.

As outlined in the discussion draft, we support the use of clearly-defined evidentiary standards for the review of requests for the qualification of surrogate endpoints. These standards should include a definition of the proposed surrogate endpoint, clear methods of assessing it in an appropriate environment, and a comprehensive description of the appropriate manner and conditions for the surrogate endpoint to be used for regulatory purposes. We support granting the Secretary the ability to consult with outside experts to assist with developing evidentiary standards and believe doing so in public forums would help ensure wide stakeholder participation and transparency in the decision-making process. We believe the legislation should make it clear that the role of outside experts is to provide information and advice to the Secretary, but the final decision on whether to accept a surrogate endpoint in a certain context remains with FDA. As the Secretary develops draft guidance proposing evidentiary standards for use of surrogate endpoints, as called for in the discussion draft, we strongly encourage consultation with basic scientists, clinical investigators, statisticians, patients, industry, healthcare providers and academia. We support the concept of a streamlined process for qualification of surrogate endpoints and would welcome the opportunity to work with the committee and the Food and Drug Administration (FDA) in its development.

Expanded Access (Sections 1211-1125)

We commend Congress and the FDA for their on-going efforts to develop processes that will assist patients to gain more timely access to emerging cancer therapeutics. These include breakthrough therapy designation, fast-track designation, priority review and accelerated approval. These approaches have expedited patient access to promising new therapies, and are helping to develop invaluable data about the safety and effectiveness of drugs and biological products made available through these mechanisms.

Recently, several states have been experimenting with legislative proposals known as "Right to Try" as a means to address frustration among patients and their families who are seeking access to experimental drugs to combat a devastating cancer diagnosis without established effective therapies. Such laws have been approved in Colorado, Michigan, Missouri, Louisiana and Arizona, and they are being considered by other states. While we understand the desire to expedite access for cancer patients to potentially beneficial therapies, we are concerned these laws are too broad and may have negative unintended consequences on the clinical trial system and the development of evidence-based therapies.

Our member organizations support the proposal in the 21st Century Cures draft that would provide for greater transparency to the public by making available the decision-making process of drug sponsors with respect to applications for expanded access to investigational drugs. The General Accountability Office (GAO) study called for in the proposal would provide an unbiased qualitative analysis of patient access to investigational drugs and provide valuable information about their potential benefit and harms to patients. The study should consider the impact not only on patients involved in the expanded access protocol, but also the impact on patients enrolled in studies and those awaiting access to safe and effective therapies. In addition, the proposed Expanded Access Task Force would develop important information that could provide greater insight on the effectiveness of current expanded access protocols, as well as recommendations on streamlining the process and making them less burdensome on doctors and sponsors. We would recommend the GAO and task force also evaluate the extent to which granting expanded access might impact the traditional drug approval process. We appreciate and support the inclusion of the patient community in this process.

Clinical Research Modernization and Centralized IRBs (Section 3001-3002)

Through advances in areas such as bioinformatics, multi-site and multi-state cancer clinical trials are becoming more commonplace. The use of single Institutional Review Boards or IRBs of Record is essential in fostering collaboration of such research efforts. For example, the NCI National Clinical Trials Network (NCTN) relies on adult and pediatric central IRBs to streamline review for NCTN studies. This has resulted in the development of consistent protocols and processes across NCTN trials, as well as cost savings to the system. This success points to the feasibility and benefits of a centralized review system, and could serve as a model for the use of single IRBs or IRBs of record for other diseases. It is essential that participating institutions agree to the approach and process, and be willing to delegate to the single IRB of record the authority to act on its behalf. For its part, the selected IRB must commit to open, regular communication with participating institutions to ensure all parties are kept informed. We believe

HHS should clearly endorse the use of a single IRB of record, with appropriate safeguards in place, so that institutions understand and appreciate it is an appropriate approach to biomedical research.

NIH Research Strategic Investment Plan (Section 4001)

Developing an NIH Research Strategic Plan to promote efficient and effective focus of biomedical research in a manner that leverages the best scientific opportunities through a deliberative planning process is a laudable goal which we support. We note that, as authorized by the National Cancer Act of 1971 (P.L. 92-218), the Director of the National Cancer Institute is charged with preparing and submitting directly to the President an annual budget for the National Cancer Program (the "Bypass Budget"). This has served as an effective mechanism for highlighting the areas of basic, clinical and translational cancer research to reduce cancer incidence, morbidity and mortality for all types of cancer. A similar NIH-wide strategic investment plan could also contribute to the goal of expanding knowledge on human health in the United States through biomedical research and include measurable objectives. Of course, any newly required strategic planning process should not be a duplication of efforts that are already underway under existing law. Additionally, we would be concerned if a designated percentage of NIH-appropriated research is devoted to a specific type of research, such as basic, clinical or translational research. We believe these decisions should be guided by scientific opportunities through a rigorous peer-review process. We would also recommend that behavioral science, which plays a vital role in cancer prevention, early detection and treatment, be a component in the development of the NIH strategic plan. While we agree that current fiscal restraints necessitate the need to avoid duplication in biomedical research, we note that multiple research efforts on similar questions or hypotheses are not necessarily duplicative in nature and are an important component of validating new discoveries. We ask that this be taken into consideration by GAO when conducting the study to evaluate duplication of federal biomedical research.

Conclusion

We are enthusiastic about your strong commitment to enhancing the nation's ability to conduct research and develop new therapies for patients. In that context, we again respectfully reiterate the severe budgetary constraints under which FDA and NIH are currently operating. New sources of funding must be identified to carry out the numerous objectives of the 21st Century Cures initiative.

NCCR appreciates the opportunity to provide these comments on the 21st Century Cures initiative. We commend and thank the bipartisan Members of Congress who have devoted their tireless efforts to developing a comprehensive framework that will greatly benefit patients, scientists and the general public. We look forward to working with Congress and the Administration on this important endeavor.

American Association for Cancer Research
American Cancer Society Cancer Action Network
American Childhood Cancer Organization

American College of Radiology
American Society of Clinical Oncology
Association of American Cancer Institutes
American Society of Hematology
Coalition of Cancer Cooperative Groups
Friends of Cancer Research
International Cancer Advocacy Network
International Myeloma Foundation
Kidney Cancer Association
LUNGevity
The Lustgarten Foundation
Melanoma Research Alliance
Pancreatic Cancer Action Network
Prevent Cancer Foundation
Prostate Cancer Foundation
Society of Gynecologic Oncologists
V Foundation for Cancer Research

National
Multiple Sclerosis
Society

May 18, 2015

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

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

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

Re: Modifications to the 21st Century Cures Act

Dear Chairman Upton and Representative DeGette:

On behalf of those Americans living with multiple sclerosis (MS), the National Multiple Sclerosis Society appreciates the opportunity to participate in this iterative dialogue on the 21st Century Cures Act. The time to revamp the medical research field is long overdue and people living with MS and other diseases are anxiously waiting for ways to expedite the process by modernizing the system and capitalizing on efficiencies.

MS – an unpredictable, often disabling disease of the central nervous system – interrupts the flow of information within the brain, and between the brain and body. Symptoms range from numbness and tingling to blindness and paralysis. The progress, severity and specific symptoms of MS in any one person cannot yet be predicted, but advances in research and treatment are moving us closer to a world free of MS.

As stated in an earlier letter to the Committee, the Society greatly appreciates that two of our major priorities were included in this bill—increased funding for the National Institutes of Health and a data collection system for neurological conditions. Below are some expanded comments on other sections of the bill.

Development

Precision Medicine Guidance (Title II, Subtitle C, Section 2041)
The Society is in favor of providing additional guidance on the precision medicine initiative and feels that the guidance will strengthen overall clinical trial design. Improving this process will be beneficial for MS research and the development of new treatments. However, the Society would like to see the initiative expanded beyond a genetic focus. Given that many diseases like MS are multi-causal, the onset of the disease is only partially attributed to genetic factors. Therefore, we encourage the Committee to expand this initiative and look for ways to incentivize analyzing lifestyle and environmental factors as well.

Adaptive Trial Design (Title II, Subtitle D, Section 2061)
The Society supports advancing the use of adaptive trials, as it could be a way to fuel the pipeline for MS drugs. Currently, the Society invests in and works closely with commercial

research entities to try to incentivize the development of MS therapies. Through this experience, the Society sees this provision as a way to additionally incentivize small businesses to engage in more MS/neuroscience drug discovery and development. Broader use of adaptive design will reduce the size of clinical trials and decrease the cost, thus allowing pharmaceutical companies to invest in additional promising agents. This is extremely important as we have seen fewer pharmaceutical investments in the neurological pipeline over the past decade.

Biomarkers, Surrogate Endpoints and Other Drug Development Tools (Title II, Subtitle A, Section 2021)
While the Society feels this section related to biomarkers and surrogate endpoints is important, there are areas we would like to see strengthened. Over the past two years, the Society has worked with the Critical Path Institute to develop a new outcome measure for MS, which has a process very similar to the one outlined in this section. Drawing on this experience, the process for validating a measure can be lengthy. Therefore, the Society encourages that the Committee suggest a timeline for this process to accelerate development. Additionally, there is a glaring lack of funding for the FDA to implement this initiative. Ideally, the Society suggests constructing a biomarker evaluation group within the FDA that has established dedicated funding. An alternative to this approach would be to task the Biomarkers Consortium to oversee this process, in order to ensure timely biomarker qualification.

Additionally, the Society was disappointed to see little mention of patient perspectives regarding clinical meaningfulness. This is particularly important in reference to biomarkers, which by definition have little or no inherent clinical meaning for patients. We encourage Congress to include a clause to mandate that patients be incorporated into the process.

Delivery

Interoperability (Title III, Subtitle A, Section 3001)
Currently, there is only a placeholder for this provision in the bill, however, the implications for this policy are vast and could improve a number of pieces of the health care system. Difficulties in sharing or “pooling” data are one of the most striking issues with our fragmented health system and create a number of research and delivery obstacles. For the patient community, the ability to access data across different systems would give providers a way to view patient information readily, while allowing researchers a way to see trends in treatment utilization. While there are likely a number of complex ways to address this issue, the Society suggests considering a phased-in mandate concerning standardization of both clinical and administrative data, which would follow the Clinical Data Interchange Standards Consortium (CDISC) standards. These standards would cover not only typical clinical data but also imaging and other biomarker and surrogate markers. This would be the first step to ensuring that the data collected is easily transmitted and mined.

On behalf of those living with MS, we thank you for the enormous effort you have invested in drafting this important piece of legislation and for soliciting our input. The Society hopes to continue being an informational resource as the bill makes its way through the legislative

National
Multiple Sclerosis
Society

process. If you have any questions or require any further information, please contact Lauren Chiarello via e-mail at lauren.chiarello@nmss.org or call 202.408.1500.

Sincerely,

Bari Talente
Executive Vice President, Advocacy
National Multiple Sclerosis Society

JOIN THE MOVEMENT

National Multiple Sclerosis Society

May 8, 2015

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

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

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

Re: Feedback on 21st Century Cures Act discussion draft version 2

Dear Chairman Upton and Representative DeGette:

The National Multiple Sclerosis Society appreciates the considerable effort the Energy and Commerce Committee has put into developing a second draft of the 21st Century Cures Act. The Society is extremely pleased that a number of our priority issues were included in this second draft and has made policy advancements that will truly accelerate the discovery and development of new treatments and cures.

While the Society is supportive of and interested in numerous scientific provisions in the legislation, the Society feels there are two components that are key to getting us closer to a cure for multiple sclerosis (MS)— collecting better information about the basis of the disease and funding the entire research pipeline.

MS—an unpredictable, often disabling disease of the central nervous system—interrupts the flow of information within the brain, and between the brain and body. Symptoms range from numbness and tingling to blindness and paralysis. The progress, severity and specific symptoms of MS in any one person cannot yet be predicted, but advances in research and treatment are moving us closer to a world free of MS.

Advancing Research through Data Collection

We thank the Committee for continuing to include this data collection system for neurological conditions in the 21st Century Cures Act draft and we fully endorse its inclusion in the final version (Title I, Subtitle G, Sec. 1122). Neuroscientists are making great strides in many areas of brain research but lack basic information about these populations to help advance their studies. In the past 40 years, there has not been a study to collect and map those people living with MS and their characteristics. The National Neurological Diseases Surveillance System would provide accurate data to researchers on incidence and prevalence, as well as risk factors, how diagnosis and treatment varies by gender, ethnicity, and region, and importantly, how these trends change over time. The

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National
Multiple Sclerosis
Society

Society's Research Advisors have stated that collecting and analyzing this data will help to advance our knowledge of neurological conditions in the future.

Funding the Entire Research Ecosystem

The Society was extremely pleased to see that one of biggest omissions in the first draft of the bill—increased resources for the National Institutes of Health (NIH)—was addressed in the second discussion draft. The Society is fully supportive of additional discretionary and mandatory funding for the NIH (Title I, Subtitle A, Sec.1001,1002). As the committee explores how and whether to fill in the authorized uses for the NIH Innovation Fund, we encourage the committee to ensure the priorities are broad enough to address many different diseases and not focus on particular conditions. Similarly, we want to reiterate from our previous comment letter that we remain concerned about the consequences of mandating a NIH strategic plan based on return on investment (Title I, Subtitle B, 1021). Determining the return on investment for discovery research is difficult and this restriction could hamstring the development of potential breakthroughs. We suggest removing that specific language.

While the committee has dedicated additional funding to boost the discovery stage of the research pipeline, the tail of the pipeline—the Food and Drug Administration (FDA)—was notably not included. In this draft of the bill, the FDA is tasked with overseeing a number of new initiatives, which includes drafting guidance. While the Society is in favor of implementing the majority of these programs, we are concerned that a lack of resources will either cause the initiatives to stall and/or have limited impact. Therefore, we encourage you to simultaneously increase investment for the FDA through appropriations, in order to ensure that the best science isn't delayed in getting to patients.

On behalf of those living with MS, we thank you for the enormous effort you have invested in drafting this important piece of legislation and for soliciting our input. The Society hopes to be a resource of information as the bill makes its way through the legislative process. If you have any questions or require any further information, please contact Lauren Chiarello via email at Lauren.chiarello@nmss.org or call 202.408.1500.

Sincerely,

[redacted]

Bari Talente
Executive Vice President, Advocacy
National Multiple Sclerosis Society

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

Dear Chairman Upton and Representative DeGette:

I wish to submit as response to the latest draft of the 21st Century Cures Act the blog that I posted to the Forbes website under the heading: "America Needs Bolder Science And The 21st Century Cures Act Should Empower It"

I am concerned that under section 1026 of the current draft, NCATS' Cures Acceleration Network (CAN) will lack the resources it needs to carry out its mission under the Act. Its mission is to spearhead the development of cures by funding higher-risk breakthrough research in areas of high potential. CAN's budget -- currently about $10 million -- has never allowed it to live up to its mission.

On the other hand, NCATS' budget will continue to fund a non-trivial amount of low-risk "safe" science whose value is marginal. To effectively manage public funds, the NCATS Director needs the authority to shift funds from low-value to higher-value research.

The initial draft of the 21st Century Cures Act gave the NCATS Director that authority, up to an amount that was envisioned to be about $100 million. This seems to better aligned with the goals of the 21st Century Cures Act, and I respectfully request that the original language be restored.

The 21st Century Cures Act is a remarkable achievement that will greatly strengthen American biomedical research, and we are thankful for your leadership in bringing it forward under sometimes difficult conditions. The small change I suggest is likely to have an outsized impact, and I hope you will consider it.

Thank you for your support of this matter.

Best regards,

Bernard Munos
Member, NCATS' Cures Acceleration Network Review Board
Member, NCATS' Advisory Council

PARKINSON'S ACTION NETWORK

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Ted Thompson, J.D.

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J. William Langston, M.D.
The Parkinson's Institute
Davis Phinney
The Davis Phinney Foundation for Parkinson's
The Honorable Janet Reno
Cokie Roberts

May 12, 2015

The Honorable Fred Upton
Chairman
Committee on Energy & Commerce
U.S. House of Representatives
Washington, DC 20515

The Honorable Frank Pallone
Ranking Member
Committee on Energy & Commerce
U.S. House of Representatives
Washington, DC 20515

The Honorable Joe Pitts
Chairman
Committee on Energy & Commerce
Subcommittee on Health
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Washington, DC 20515

The Honorable Gene Green
Ranking Member
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Subcommittee on Health
U.S. House of Representatives
Washington, DC 20515

The Honorable Diana DeGette
Ranking Member
Committee on Energy & Commerce
Subcommittee on Oversight & Investigation
U.S. House of Representatives
Washington, DC 20515

Dear Chairmen Upton and Pitts and Ranking Members Pallone, Green, and DeGette,

On behalf of the Parkinson's Action Network (PAN), thank you for your continued work on the 21st Century Cures Initiative. We commend you for including a top priority of the Parkinson's community, the National Neurological Diseases Surveillance System, in the current draft legislation and for supporting medical research at the National Institutes of Health (NIH). As you move forward with consideration of the *21st Century Cures Act*, we urge you to provide additional funding for the Food and Drug Administration (FDA) so the agency has the resources necessary to ensure successful implementation of 21st Century Cures.

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 Americans living with Parkinson's disease, for whom there is no treatment available that slows, reverses, or prevents progression.

National Neurological Diseases Surveillance System (Section 1122)
Thank you for the inclusion of Section 1122, the National Neurological Diseases Surveillance System. We estimate that between 500,000 to 1.5 million Americans are living with Parkinson's disease but we do not have accurate information on how many

are actually battling Parkinson's, and what causes the disease. This lack of core knowledge inhibits Parkinson's research, treatments, programs, and services. A national neurological surveillance system at the Centers for Disease Control and Prevention (CDC) will provide data on the epidemiology, incidence, and prevalence of neurological diseases. Better data would allow for future planning of health care needs, detect changes in health practices, assess disease burden, promote education about neurological diseases, and, most importantly, support a wide range of research initiatives. We strongly support this provision and hope it will remain in the final legislation presented to Congress and ultimately signed into law.

NIH Innovation Fund (Section 1002)

PAN also commends you for including a $10 billion NIH Innovation Fund for research supported by NIH as well as authorized spending increases for the Agency. The federal government plays a critical role in funding research and development of new treatments for Parkinson's, as well as other chronic conditions, and we are pleased the Committee has made NIH funding a priority in the current draft. For clarification as to how and when the Fund would be triggered, we recommend the Committee designate a baseline appropriations level that is equal to the amount received by NIH under regular budget authority in Fiscal Year 2015. While we understand the resources allocated will be authorized for only certain uses, including precision medicine and young emerging scientists, we strongly encourage you to expand its reach to allow the fund to support broad investigator initiated grants that could support a wide variety of research activities and priorities.

Additional Support for the FDA

Support of medical research at NIH is a great step forward; however, we are concerned the Committee did not provide additional funding for the FDA. Given the addition of many mandates, reports, and other responsibilities, additional appropriated funding should be made available to ensure the Agency has the ability to not only continue their important day-to-day work but also has the resources, staff, and expertise available to implement the new provisions. We remain concerned that without additional funding for FDA, implementation and overall capacity of the Agency will suffer. We urge the Committee to work with Appropriators to include a commitment to sustainable and predictable funding for the FDA.

Thank you again for your leadership and your continued progress on this exciting initiative. If you have any questions, please contact Jennifer Sheridan Palute, PAN's director of policy, at jpalute@parkinsonsaction.org or 202-638-4101 ext. 112.

Sincerely,

Ted Thompson, J.D.
Chief Executive Officer

PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE

May 12, 2015

The Honorable Fred Upton
The Honorable Frank Pallone
The Honorable Joe Pitts
The Honorable Gene Green
The Honorable Diana DeGette
Committee on Energy and Commerce
United States House of Representatives
2125 Rayburn House Office Building
Washington, DC 20515

Dear Representatives Upton, Pallone, Pitts, Green and DeGette:

The Patient-Centered Outcomes Research Institute (PCORI) applauds the efforts of the House Energy and Commerce Committee to forge a bipartisan approach to speeding development of effective new therapies and to involving patients in the process. PCORI has proven that involving patients leads to research questions and study procedures that are more salient and relevant to patients. We agree that engaging patients will improve the entire research pathway from scientific discovery to optimal healthcare, and PCORI stands ready to help.

I am pleased to respond to your request to provide PCORI's comments on the second Discussion Draft entitled the "21st Century Cures Act," released on April 29, 2015. As you know, PCORI is an independent, nonprofit organization that funds research to improve the quality and relevance of evidence available to help clinical decision makers — patients, caregivers, clinicians, employers, insurers, and policy makers — make better-informed health care decisions.

PCORI's legislatively mandated mission is to support research to determine which therapies work best for individual patients across a wide range of illnesses and conditions. Specifically, we fund research that can identify instances where a treatment works for some patients but not others and we can then study those in whom it does not work, looking at both genetic and non-genetic factors such as age, gender, race-ethnicity and concurrent illnesses. The results of our research can help identify novel disease mechanisms and pathways that can lead other entities to develop new, more effective therapies. At the other end of the development cycle, PCORI-funded comparative clinical effectiveness research (CER) can evaluate more precisely how new medicines work and under what circumstances new treatments are superior to existing approaches.

Our comments on the second draft, found below in *italics*, are focused primarily on areas of the draft that are new or where we did not comment previously.

TITLE II – DEVELOPMENT

Subtitle - A Patient-Focused Drug Development

Sec. 2001. Development and use of Patient Experience Data to Enhance Structured Risk-Benefit Assessment Framework

The goal of this section is ensure greater involvement by patients in the drug development process. Specifically, the Secretary is required to establish a process so that an entity seeking to provide patient experience data must follow a set of steps for it to be used in the risk-benefit assessment framework. This section also requires biannual workshops on the methodology of patient experience data.

Although PCORI is not involved in the phase of research related to drug development, the core of our mission is to include patients and other stakeholders in the healthcare system in our research so that it is useful, attentive to patient preferences and circumstances, and rapidly disseminated to improve practice. Since our inception, we have funded 50 pilot projects to determine the most effective ways to engage patients and stakeholders in research, we continually monitor and evaluate how patients and stakeholders are involved in our research programs, and we produced a Methodology Report and standards that provide baseline requirements and a framework for most effective practices in the planning, design, and conduct of patient-centered outcomes research.

Our National Patient-Centered Clinical Research Network (PCORnet), initiated in 2014, is comprised of 29 constituent networks, 18 of which are Patient-Powered Research Networks (PPRNs), which are operated and governed by patient-led groups. All 29 networks involve patients in governance of network activities. Patients help to generate research questions and approve participation of their network within each multi-network study. In addition, patient partners work with health systems, researchers and other patients in addressing issues of patient privacy in the use of stored electronic clinical data. PCORI's previous efforts and experience in this area should be helpful in guiding the collection and methodological work around gathering patient data, and we are very happy to be a resource in any way we can, for example, through our PCORnet patient community.

Subtitle C – FDA Advancement of Precision Medicine

Sec. 2014. Precision Medicine Guidance and Other Programs of FDA (Bracketed)

This section describes precision medicine, provides general agency guidance, its use in orphan drugs and expedited approval programs.

The Precision Medicine Initiative will need multiple precisely-defined cohorts to achieve its potential of predicting health, disease course and treatment response, improving diagnosis of illness, and identifying new targets for therapies for a variety of conditions. Because different questions require different cohorts (e.g., defined by disease, severity, or race/ethnicity) and different data, "mega cohorts" may be needed to answer many important questions quickly and at low cost.

To address the challenges of assembling large research-ready cohorts, the FDA and NIH should take advantage of existing very large cohorts that include standardized electronic health data, and where available, genetic data and biologic samples, developed through partnerships of patients, investigators, clinicians, and health systems. Multiple cohorts of different sizes can then be drawn from these larger, well-characterized populations for which analysis-ready data already exists, and for which established mechanisms exist to engage individuals and their providers.

PCORI's Patient-Centered Outcomes Research Network (PCORnet) is an existing research "meta-network" that includes 11 Clinical Data Research Networks (CDRNs) representing more than 150 health systems that are transforming electronic health record, claims, and patient-reported data on a general population of 1 to 14 million persons per CDRN into a common data model (CDM) and, as noted above, 18 Patient-Powered Research Networks representing highly engaged patients from 93 different common and rare disease groups who are willing to share their data. Collectively, PCORnet includes participants from all 50 states, representing both general and disease-specific cohorts of patients. The PCORnet Coordinating Center enables "one-stop entry" for sponsors and others seeking to use PCORnet. PCORnet is developing policies requiring use of a central IRB as well as a master contract agreement to streamline study participation.

A variety of conditions could be studied within PCORnet with great precision and attentiveness to what works for different population subgroups. PCORnet patients are highly representative of the US population, its race/ethnic composition, socioeconomic status, and age distribution. PCORnet is developing the capability to use EHR data to rapidly identify patients with over 90 unique conditions. Networks can identify and contact patients based on electronic health data using web portals, email, phone, face-to-face recruitment, and mobile platforms. Patients can be electronically consented for observational and interventional studies, including the collection of additional biospecimens and patient-reported data as needed.

Finally, PCORI's broad and deep connections with dozens of patient communities can help increase awareness of the importance of precision medicine.

Sec. 505H. Utilizing Evidence from Clinical Experience (Bracketed)

The purpose of this section is to establish a program to evaluate the "potential use of evidence from clinical experience" to 1) "help support the approval of a new indication for a new drug," or 2) "help support or satisfy post-approval study requirements." Clinical experience is defined as information from sources other than randomized clinical trials. The framework should include the "current sources of data development," including "patient-centered outcomes research activities," gaps in data collection, among other activities, and provide guidance to the Secretary regarding when this evidence can be used and how it should be collected.

PCORI is very supportive of such a program to evaluate medical care through the lens of real-world, clinical experience. As we noted in a recent PCORI blog post, "not all patients will react to a medical treatment in the same way. A treatment that works well for some patients may be ineffective, or even harmful, for others. And that often makes it difficult for patients and clinicians to make informed health and healthcare decisions." Since many studies only provide evidence of an average effect of a treatment vs. a specific effect, it is imperative that the nation leverage more data from the care delivered daily in clinical settings across the country.

*Such a program can include information derived from EHRs, but also, importantly patient-**reported** outcomes data. Our PCORI Methodology Report includes recommendations on many of the topics identified in this section of the discussion draft, including standards for identifying gaps in the evidence so that appropriate research questions may be formulated. It also includes standards for identifying and recruiting an appropriately representative population, as well as a standard for including patient-reported outcomes when patients themselves are the best source of information about a given treatment. For PCORI-funded studies that are specifically examining the variability, or heterogeneity of treatment effects across a population, our methodology standards require researchers to clearly indicate the methods used to assess this variability so that others can understand and apply the insights.*

PCORI's commitment to using evidence from real-world clinical experience and our Methodology Standards regarding patient recruitment and patient-reported outcomes can be significant resources for the development of a framework that will include current sources of data, gaps, current standards and methodologies and remaining challenges. Given our focus, we can be particularly helpful in helping to support or satisfy post-approval study requirements.

Sec. 5051. Collecting Evidence from Clinical Experience through Targeted Extensions of the Sentinel System (Bracketed)

The section requires the Secretary to establish pilot demonstrations between data captured through the Sentinel System and complementary public health data, along with a "governance mechanism and operational guidelines for the collection analysis and use of such data intended to generate evidence from real world clinical experiences to improve assessment of benefit-risk, protect public health and advance patient-centered care."

The FDA Sentinel System is designed to monitor the safety of FDA-regulated medical products by using existing electronic healthcare data from multiple sources, including administrative claims submitted by healthcare providers to insurance companies. The goals of the Sentinel System, to provide an active safety surveillance system for the FDA, and PCORnet, to provide an infrastructure to conduct patient-centered comparative effectiveness research for PCORI, are complementary in that each can contribute to a better understanding of the complete experience of care. PCORnet and the Sentinel System collaborate closely, as the Coordinating Center Principal Investigator for PCORnet is also the Sentinel System Coordinating Center Principal Investigator. Early on, we recognized the need to explore and demonstrate the opportunities for data linkage, and we have a manuscript in preparation that further builds

on and describes this opportunity. At its essence, this manuscript observes the overlapping need for both PCORnet and Sentinel in the need for longitudinal integrated clinical data. Neither clinical/EHR data alone, nor data from administrative claims alone, are sufficient to address the full breadth of patient-centered comparative clinical effectiveness research. PCORI would be enthusiastic about working with the Secretary to establish pilot demonstrations and share our experience related to governance principles and processes that guide data linkage.

Many thanks for giving PCORI an opportunity to comment on the second discussion draft. We would be happy to answer any questions, clarify any of our comments, or provide additional information as your work on the 21st Century Cures draft continues.

Sincerely,

Joe V. Selby, MD, MPH
Executive Director
Patient-Centered Outcomes Research Institute (PCORI)
1828 L Street, NW 9th Floor, Washington, DC 20036

P•C•R•C

PHYSICIAN CLINICAL REGISTRY COALITION

February 19, 2015

Via Electronic Mail (Corrected)

The Honorable Fred Upton
Chairman
House Energy & Commerce Committee
U.S. House of Representatives
2125 Rayburn House Office Building
Washington, D.C. 20515
cures@mail.house.gov

Dear Chairman Upton:

The undersigned members of the Physician Clinical Registry Coalition applaud the Energy and Commerce Committee for issuing the 21st Century Cures discussion document (the Discussion Document or Document) to advance public discussion about the pace of cures in the United States. We are particularly pleased with the Document's focus on ways to encourage and facilitate the development and effectiveness of clinical data registries.

The Physician Clinical Registry Coalition (Coalition) represents 21 national medical specialty societies and other physician-led groups that sponsor clinical data registries that collect and analyze clinical outcomes data to identify best practices and improve patient care. Many of the members of the Coalition have been approved by the Centers for Medicaid and Medicare Services (CMS) as Qualified Clinical Data Registries (QCDRs) or Qualified Registries, or are in the process of seeking such approval, under the Physician Quality Reporting System (PQRS) program. We, therefore, appreciate the opportunity to submit these comments on the provisions of the Discussion Document that affect the development or operation of clinical data registries.

We are attaching a copy of the Coalition's recently-released *Guidance on Legal Challenges and Regulatory Obligations for Clinical Data Registry* ("*Legal Challenges Guidance*"). We hope this paper provides useful background information for the Committee's work to identify ways that Congress can help to alleviate unnecessary burdens and facilitate medical innovation.

The Discussion Document includes several provisions that relate to clinical data registries; yet, as the document indicates, there is currently no statutory definition of a clinical data registry outside of the Medicare program's definition of a QCDR. We suggest the Committee consider adopting the following definition of clinical data registries, loosely based on the definition set forth in the registries user guide published by the Agency for Health and Research Quality (AHRQ)[1]:

A clinical data registry is an organized data collection system operated by or affiliated with a medical society, hospital association, or other health care association, that collects uniform data (clinical and other) to evaluate specified outcomes for a population defined by a particular disease, condition, or exposure, and that serves one or more predetermined scientific, clinical, or policy purposes, including but not limited to describing the natural history of disease; determining clinical effectiveness or cost effectiveness of health care products and services; measuring or monitoring safety and harm; and/or measuring quality of care.

We are aware that there may be other definitions and are happy to work with the Committee and other groups to refine this definition.

The remainder of this letter provides our specific comments on the sections of the Discussion Document that most directly affect clinical data registries.

[1] Gliklich R, Dreyer N, Leavy M, eds., *Registries for Evaluating Patient Outcomes: A User's Guide*. Third edition. Two volumes. (Prepared by the Outcome DEcIDE Center [Outcome Sciences, Inc., a Quintiles company] under Contract No. 290 2005 00351 TO7.) AHRQ Publication No. 13(14)-EHC111. Rockville, MD: Agency for Healthcare Research and Quality. April 2014, Vol. 1, p. 1. http://effectivehealthcare.ahrq.gov/ehc/products/420/1897/registries-guide-3rd-edition-vol-1-140430.pdf.

1. EXPANDING USES OF MEDICARE DATA BY QUALIFIED ENTITIES—Section 2085(a)

The Coalition supports the provisions of Section 2085(a)(2)(A)(ii) that allow qualified entities to share Medicare data with individual health care providers and medical societies for quality of care improvement purposes and at no cost to such authorized users. These data may only be shared for nonpublic uses. We encourage the Committee to make this section even stronger by *requiring* qualified entities to share these data with providers and medical societies, rather than making data sharing discretionary. We also ask that the Committee clarify the meaning of "nonpublic use" and the preclusion in subparagraph (3)(C) on use of data provided by qualified entities for marketing purposes. We would like to make sure these restrictions would not prevent medical societies from sharing data with their participants or other parties for purposes of quality improvement or research, or from posting analyses on the society's website to promote public awareness of the registry's work.

In addition, we urge the Committee to require the Secretary to include verification of life status as part of the claims data provided by CMS to qualified entities under 42 U.S.C. § 1395kk(e) and by qualified entities to medical societies and other authorized users under this section. Utilizing clinical data, combined with claims information and death status would allow many medical society clinical data registries to provide long-term information on patient treatment outcomes and estimate patient survival rates. Physicians, hospitals, and other clinical registry participants can use this information to evaluate their respective outcomes against national standards or benchmarks. Outcomes data linked with death status data also help physicians, patients, and their families make informed treatment decisions. Clinical data registries and their participants can also use this information to facilitate research comparing the long-term effectiveness of alternative treatment strategies based on patient demographics.[2]

[2] We understand that the current statutory framework (*i.e.*, Section 205(r) of the Social Security Act, 42 U.S.C. § 405(r)) presents some challenges to the Secretary's ability to share state death data from the Social Security Death Master File, but are confident that this data sharing/linking could be accomplished under Section 205(r)(9), 42 U.S.C. §405(r)(9), of that Act.

2. ACCESS TO MEDICARE DATA BY QCDRS—SECTION 2085(b)

We strongly support the proposal to require the HHS Secretary to make Medicare, Medicaid, and CHIP claims data available to QCDRs and would urge the Committee to make these data available to clinical data registries generally. While many organizations that operate clinical data registries have obtained QCDR status for one or more of their databases, many registries have not obtained QCDR status. Indeed, some medical societies have one database that has qualified as a QCDR, but others that have not. It is imperative for many clinical data registries, and not just QCDRs, to have access to Medicare, Medicaid, and CHIP claims data to enhance their ability to track patients over time and therefore better analyze outcomes from surgical and other medical procedures.

We urge the Committee to require the Secretary to include verification of life status as part of the claims data provided under this section for the same reasons stated in our comments on Section 2085(a) above.

We also do not believe that registries should be required to pay for access to these data. Most registries are sponsored by nonprofit organizations and many have limited budgets. Moreover, the studies that clinical registries conduct using federal program data are typically used to support public purposes and specific public policies, including CMS reimbursement and coverage policies, Food and Drug Administration pre- and post-market surveillance programs, and other government initiatives. Allowing the Secretary to charge clinical data registries a fee for access to program data is inconsistent with the language of Section 2085(a)(2)(C), which precludes qualified entities from charging authorized users a fee for supplying them with Medicare data. We ask that the Committee remove the fee requirement or at least give the Secretary the discretion to reduce or waive the fee if the data are being used to support public purposes/policies.

3. HIPAA COMMON RULE EXCEPTION—Section 2087

The Coalition strongly supports the inclusion of language requiring the Secretary to establish an exception to the Common Rule that allows clinical data registries to comply with the privacy and security provisions of the Health Insurance Portability and Accountability Act of 1996 instead of comparable provisions of the Common Rule. The need for this exception is discussed in our *Legal Challenges Guidance* (at pp. 7-8).

The Common Rule applies to entities involved in human subjects research that receive federal funding and/or engage in federally-regulated activities, including most teaching hospitals and academic medical centers—the prime participants in most clinical data registries. The Common Rule's requirements for the use and disclosure of patient data are generally also covered by HIPAA rules that are far more protective of patient privacy. Uncertainty over the applicability of the Common Rule and duplicative requirements are imposing unnecessary burdens among hospitals and other current and prospective registry participants.

We would suggest that the Discussion Document be more specific and give the Secretary more direction on the nature and scope of this exception. Specifically, we recommend that, at a minimum, the exception apply in situations where clinical data registries are collecting identifiable patient information, but are not engaged in direct human subjects intervention or interaction for research purposes (*e.g.*, clinical studies), and are following all the applicable requirements of the HIPAA regulations with respect to protecting the privacy and security of such information. These are the situations where the Common Rule's duplicative and burdensome requirements create the most confusion and other problems for registries and their participants. The exception would not apply to registries, participants, or other entities conducting research that involves direct interaction with patients for purposes of such research, rather than simply for purposes of clinical care or quality improvement.

To implement this recommendation, we suggest you replace Section 13431(2) (p. 183, lines 23-26 through p. 184, lines 1-3) with the following two new paragraphs:

> (2) establish an exception to the provisions cited in paragraphs (1)(A) and (B) for clinical data registries that are collecting individually identifiable health information, as defined by 42 C.F.R. 160.103, but are not engaged in direct intervention or interaction with human subjects for research purposes and are following all the applicable requirements of the privacy and security rules issued under the Health Insurance Portability and Accountability Act of 1996, as amended, [Pub. L. No. 104-191, 110 Stat. 1936 (1996) (codified at 42 U.S.C. § 1320d *et seq.*)], with respect to such information.

(3) issue guidance on the remaining applications of the provisions cited in paragraphs (1)(A) and (B) to clinical data registries within one year after the date of enactment of this section.

4. COMMISSION ON DATA SHARING FOR RESEARCH AND DEVELOPMENT—Section 2091

The Commission on Data Sharing for Research and Development created under this section is charged with establishing various standards, processes, procedures, and best practices for the collection and dissemination of clinical data by clinical data registries. We strongly support the identification and promotion of best practices for clinical data registries. Such efforts are critical to ensuring the integrity and effectiveness of registry processes. We also generally support the specific registry practices identified in this section as being among those that are worthy of review and guidance.

The development of best practices should emanate from the clinical data registry community rather than the federal government. The government's role should be to recognize and promote innovative practices by clinical data registries and ensure that the technological and legal infrastructures support those efforts.

Although the Discussion Document does not give the Commission power to enforce the standards it sets, the language describing the Commission's charge seems prescriptive, rather than advisory, and the Commission actions could easily be given the force of law through regulations issued by various agencies within HHS. We would encourage the Committee to revise this section to form a true advisory body that is selected in a non-partisan fashion and that includes a wide range of stakeholders from and nominated by the clinical data registry community. The mission of the advisory body should be to highlight best practices by clinical data registries and be a source for the Secretary's recommendations in Section 2092. Together, the Secretary and the registry advisory body can work to identify and promote best practices, establish the infrastructure for registry data collection and sharing (*e.g.*, interoperability with EHRs), safeguard patient privacy and security, and protect registry data from legal discovery.

5. RECOMMENDATIONS FOR DEVELOPMENT AND USE OF CLINICAL REGISTRIES—Section 2092

This section directs the Secretary to make recommendations for the development and use of clinical data registries and their integration with clinical practice guidelines and best practices or standards of care. The Coalition supports this provision, particularly to the extent that it addresses the promotion of bidirectional, interoperable exchange of information between electronic health records (EHRs) of reporting clinicians and registries. Extraction of clinical data from EHRs is the most efficient method of collecting data. But, the lack of interoperability between EHRs and clinical data registries is a serious impediment to this data collection method. Indeed, we would favor even stronger language requiring the Secretary to adopt and issue interoperability standards, implementation specifications, and/or certification criteria to ensure meaningful and timely exchange of information between certified EHRs and clinical data registries. In addition, meeting these interoperability standards should be a condition of certification for EHR technology for "Meaningful Use" purposes.

We are also concerned that the recommendations for interoperability are conditioned on adoption by clinical data registries. In fact, the principal impediment to integration of EHR data into clinical data registries is that some EHR companies refuse to share their data with registries or are charging their customers or registries excessive fees for this data exchange. As noted above, these standards need to be mandated by the Secretary for adoption by EHR companies as a condition of certification for EHR technology. EHR companies also should not be able to charge their customers or clinical data registries for sharing their customers' data with registries.

We strongly support the requirement in subparagraph (c) that the Secretary consult with national medical societies when developing these recommendations. We encourage the Committee also to require the Secretary to consult with clinical data registries directly since many such registries are not tied to a particular medical society or are managed separately from such societies.

6. SUGGESTED ADDITIONAL ISSUES

a. Protection from Legal Discovery

We would urge the Committee to add a section to the Discussion Document protecting clinical data registry data from legal discovery, particularly data that identifies or could identify specific patients, providers, or facilities. There is currently no adequate federal protection for such data from subpoenas or other litigation-related discovery requests. The risk that such data may be

subject to forced disclosure creates a chilling effect on the ability of clinical data registries to recruit data sources. Patient and provider-identifiable data collected by clinical data registries should be afforded the same or similar protections/privilege as "patient safety work product" submitted to Patient Safety Organizations (PSOs) under Section 922 of the Patient Safety and Quality Improvement Act.[3] Clinical data registries generally don't fall within the definition of a PSO under this Act or the implementing regulations issued by AHRQ. Even when they do, clinical data registries should not need to be reconfigured to become PSOs and subject themselves to the multitude of PSO rules and regulations simply to protect their data from legal discovery. This issue is discussed in detail in our *Legal Challenges Guidance* (at pp. 12-18). We would be happy to work with Committee staff in developing the language for this privilege.

b. Group Practice Option for QCDR Reporting

Section 601(b)(1) of the American Taxpayer Relief Action of 2012[4] directed the Secretary to create an option for eligible professionals to satisfy the Physician Quality Reporting System (PQRS) incentive payment and penalty-avoidance requirements by reporting through a QCDR. CMS has interpreted the reference to "eligible professional" to preclude it from providing a PQRS QCDR group practice option. CMS permits several other options for group practice reporting, so there is no reason for not providing a QCDR group reporting option except for the apparent limitation of the authorizing statute. Accordingly, we urge the Committee to add language to the Discussion Document that would amend the QCDR authorizing legislation to permit group reporting by QCDRs. The following revisions to subparagraph D of the QCDR legislation would accomplish this purpose:

> (D) SATISFACTORY REPORTING MEASURES THROUGH PARTICIPATION IN A QUALIFIED CLINICAL DATA REGISTRY.—For 2014 and subsequent years, the Secretary shall treat an eligible professional and group practices (as that term is defined by the Secretary) as satisfactorily submitting data on quality measures under subparagraph (A) if, in lieu of reporting measures under subsection (k)(2)(C), the eligible professional or group practice is satisfactorily participating, as determined by the Secretary, in a qualified clinical data registry (as described in subparagraph (E)) for the year.

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[3] Pub. L. No. 109-41, Section 922 (codified at 42 USC § 299b-22).
[4] Pub. L. No. 112-40, Title VI, Subtitle A, Section 601(b)(1) (codified at 42 U.S.C. 1395w–4(m)(3)).

We appreciate the opportunity to submit these comments and would be happy to meet with Committee staff to discuss any of the sections of the Discussion Document that affect clinical data registries and/or QCDRs. If you have questions or would like to arrange a meeting, please contact Rob Portman of Powers Pyles Sutter & Verville at 202-872-6756 or rob.portman@ppsv.com.

Sincerely,

AMERICAN ACADEMY OF DERMATOLOGY ASSOCIATION
AMERICAN ACADEMY OF NEUROLOGY
AMERICAN ACADEMY OF OPHTHALMOLOGY
AMERICAN ACADEMY OF PHYSICAL MEDICINE AND REHABILITATION
AMERICAN ASSOCIATION OF NEUROLOGICAL SURGEONS
AMERICAN COLLEGE OF EMERGENCY PHYSICIANS
AMERICAN COLLEGE OF SURGEONS
AMERICAN GASTROENTEROLOGICAL ASSOCIATION
AMERICAN JOINT REPLACEMENT REGISTRY
AMERICAN SOCIETY FOR RADIATION ONCOLOGY
AMERICAN SOCIETY OF CLINICAL ONCOLOGY
AMERICAN SOCIETY OF NUCLEAR CARDIOLOGY
AMERICAN SOCIETY OF PLASTIC SURGEONS
AMERICAN UROLOGICAL ASSOCIATION
ANESTHESIA QUALITY INSTITUTE/AMERICAN SOCIETY OF ANESTHESIOLOGISTS
GIQUIC/ AMERICAN COLLEGE OF GASTROENTEROLOGY
NATIONAL ASSOCIATION OF SPINE SPECIALISTS
SOCIETY OF INTERVENTIONAL RADIOLOGY
SOCIETY FOR VASCULAR SURGERY
SOCIETY OF NEUROINTERVENTIONAL SURGERY
THE SOCIETY OF THORACIC SURGEONS

SAREPTA
THERAPEUTICS

May 15, 2015

The Honorable Fred Upton, Chairman
The Honorable Frank Pallone, Ranking Member
The Honorable Diana DeGette
Committee on Energy and Commerce
United States House of Representatives
2125 Rayburn House Office Building
Washington, DC 20515

Re: Comments on the 21st Century Cures Act

Dear Chairman Upton, Ranking Member Pallone and Representative DeGette:

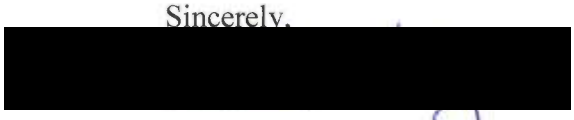
Thank you and the Committee on Energy and Commerce for its leadership on the 21st Century Cures Initiative and the opportunity for patient groups, academia and industry to play an ongoing part in the legislative development process. We commend your efforts leading to the release of the latest legislative draft of the 21st Century Cures Act and its successful markup on May 14, 2015 by the Subcommittee on Health. The draft legislation truly reflects your hard work to advance meaningful policies to improve drug development and make a difference in the lives of patients and families affected by rare diseases.

In particular, we are immensely supportive of your continued inclusion of language to clarify FDA's authority to extrapolate data in reviewing therapies for rare diseases which often comprise ever smaller – and difficult to study – patient subpopulations. Section 592 ("Precision Medicine Regarding Orphan Drug and Expedited Approval Programs") aims to ensure FDA's regulatory policies keep pace with the development of innovative precision therapies that target rare diseases for serious conditions. The language clarifies and underscores FDA's discretionary authority to expedite development of precision drugs by relying upon extrapolated data from previously approved drugs that use the same or similar approach. For patients and innovators alike, Section 592 provides a necessary signal that a viable regulatory pathway exists that can overcome the difficulties of doing conventional trials for many extremely rare conditions and offers the promise of spurring the streamlined development of much needed treatment options.

We are also pleased to see many provisions in the latest draft legislation that hold promise for the rare disease community – to include efforts to incorporate patient perspectives, modernize clinical trials, encourage greater use of post-market and real-world data, and enhance FDA's scientific capacity.

As the legislation moves forward, we are committed to continuing to work with your Committee, the Senate, the FDA and all external stakeholders to advance this critical policy in a way that will achieve maximum benefit to the rare disease patient community.

Sincerely,



Edward M. Kaye, M.D.
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May 18, 2015

The Honorable Fred Upton, Chairman
Energy and Commerce Committee
U.S. House of Representatives
Washington, DC 20515

The Honorable Diana DeGette
U.S. House of Representatives
Washington, DC 20515

Dear Chairman Upton and Representative DeGette:

As the nation's largest private funder of childhood cancer research (second only to the U.S. government) and a volunteer-driven organization committed to funding promising research to discover cures for childhood cancers and that would ensure survivors long and healthy lives, the St. Baldrick's Foundation is proud to support Sections 2082 and 2083 proposed by Congressman Michael McCaul. We are writing to express our support for the efforts to increase transparency and effectiveness of compassionate use programs. This is an issue that is critical to the childhood cancer community. A clear and understandable process for parents and physicians is vital to apply for compassionate use in a timely manner. We applaud Congressman McCaul's efforts to create a well-defined pathway for families to apply and create a better understanding of compassionate use programs provided by companies.

St. Baldrick's Foundation is committed to the clinical trials process and its vital role in discovering cures for our children. We want to make sure the process for compassionate use is well understood by the childhood cancer community, the role of compassionate use programs, and to ensure the safety of all children with cancer.

We would welcome an opportunity meet with you to discuss this section of the bill and other issues, including the important role of the St. Baldrick's Foundation in funding childhood cancer research.

Sincerely,

Danielle D. Leach, MPA
Director of Government Relations and Advocacy
Danielle.Leach@stbaldricks.org
571-388-7113

Tulane University

SCHOOL OF MEDICINE

L. Lee Hamm, MD
Senior Vice President & Dean, School of Medicine
James R. Doty Distinguished Professor and Chair

May 14, 2015

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

Dear Chairman Upton:

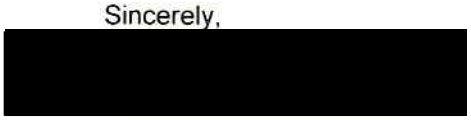
On Behalf of the Tulane School of Medicine, I am writing to thank you for your efforts on 21st Century Cures legislation and to express our gratitude for the efforts to strengthen funding for the National Institutes of Health (NIH). Your work, and the work of the Members on the Committee, to move this legislation forward is greatly appreciated.

Efforts to authorize and provide increased funding for the NIH, including $10 billion over the next five years in mandatory funding through an NIH Innovation Fund, is especially important as Tulane is a leader in biomedical research through our School of Medicine and School of Public Health and Tropical Medicine. Funding from NIH is helping Tulane make important strides in research to improve healthcare for chronic disease, especially for underserved populations; enhance aging research; support young scientists in biomedical research; and move toward better detection and treatment of infectious diseases. However, over the last decade NIH funding has remained flat, jeopardizing promising research, which is why your leadership of the 21st Century Cures Initiative is critical.

We are pleased with the bipartisan efforts that have gone into 21st Century Cures legislation. This legislation provides us with optimism that Congress is serious about the need to accelerate the development of cures by bolstering the biomedical research enterprise.

Thank you again for your efforts.

Sincerely,



L. Lee Hamm, MD
Senior Vice President & Dean, School of Medicine
The James R. Doty Distinguished Professor and Chair

LLH/dlg

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UC San Diego
HEALTH SCIENCES

May 6, 2015

The Honorable Fred Upton, Chairman
Committee on Energy and Commerce
125 Rayburn House Office Building
Washington, D.C. 20515

Dear Chairman Upton,

I am just delighted that the Energy and Commerce Subcommittee on Health has called for $10 billion for National Institute of Health (NIH) mandatory funding. I am deeply excited that the subcommittee recognizes the importance of maintaining NIH funding as a national priority. It is critically important that our nation stays competitive while sustaining leadership in medical research. NIH funded research is essential in the effort to sustain and compete in today's innovative global economy. It is important to remain focused on the common goal of helping patients, and finding "breakthrough" drugs that show promise in treating life threatening diseases. I applaud you for championing this landmark provision.

Sincerely,

Jack E. Dixon, PhD
Professor of Pharmacology, Cellular and Molecular Medicine, Chemistry and Biochemistry
Associate Vice Chancellor – Scientific Affairs

cc: Dr. David Brenner, Vice Chancellor – Health Sciences
Paul Viviano, Associate Vice Chancellor

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USAgainstAlzheimer's
we can stop it by 2020.

1101 K Street, NW | Suite 400 | Washington, DC 20005
202.360.2043 | usagainstalzheimersnetwork.org

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 regarded 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