

## **NAMI Responses to the House Energy & Commerce 21<sup>st</sup> Century Cures Proposal**

On behalf of the National Alliance on Mental Illness (NAMI), I am pleased to offer our responses to the recent solicitation from the Energy & Commerce Committee on the bipartisan 21<sup>st</sup> Century Cures initiative.

NAMI is the nation's largest grassroots advocacy organization representing persons living with serious mental illnesses and their families. Through approximately 1,000 affiliates in all 50 states, we support education, outreach, advocacy and research on behalf of persons with serious mental illnesses such as schizophrenia, manic depressive illness, major depression, severe anxiety disorders and major mental illnesses affecting children.

An estimated 11.5 million American adults live with a mental illness that is often seriously disabling, such as schizophrenia, bipolar disorder, and major depression. Based on estimates for 2010, mental illnesses accounted for 21.3% of all years lived with disability in the United States. Among the top 20 causes of years lived with disability, five were mental illnesses: major depressive disorder (8.3% of the total), anxiety disorders (5.1%), schizophrenia (2.2%), bipolar disorder (1.6%) and dysthymia (1.5%). Suicide is the 10th leading cause of death in the US, accounting for the loss of more than 38,000 American lives each year, more than double the number of lives lost to homicide. The social and economic costs associated with these illnesses are tremendous. A cautious estimate places the direct and indirect financial costs associated with mental illness in the U.S. at well over \$300 billion annually, and it ranks as the third most costly medical condition in terms of overall health care expenditure, behind only heart conditions and traumatic injury.

Mental illness and substance abuse disorders account for more than 20 percent of overall national disability and mortality. However, our overall national investment in research on these disorders is lagging. The budget of National Institute of Mental Health (NIMH) is less than 5 percent of the NIH budget, the National Institute on Drug Abuse (NIDA) budget is less than 4 percent – less than half of what would be expected if NIH funding was allocated based on the consequences of the public health burden of specific illnesses.

Moreover, these costs are not only financial, but also human in terms of lost productivity, lives lost to suicide and broken families. Investment in mental illness research and services are – in NAMI's view – the highest priority for our nation, Congress and the Energy & Commerce Committee as you consider 21<sup>st</sup> century cures.

### ***What is the state of discovery of cures and treatment for your disease? Are there cures and treatment on the horizon?***

The reality is that the current treatments available for serious mental illnesses such as schizophrenia and bipolar disorder are palliative interventions, not curative. At their most optimal and effective use, they are able to improve functioning and allow some to experience

recovery and community integration. For major mental illnesses, we are still waiting for discreet novel interventions that can genuinely change the course of the illness and avoid lifelong disability and impairment. This includes development of a new third generation of antipsychotic medications to treat psychotic disorders.

In NAMI's view, it is critical for us to move beyond the current universe of palliative treatments for serious mental illness. The sad fact is that even with optimal care, some children and adults living with serious mental illness will not be able to achieve recovery (as defined as permanent remission). People living with serious mental illness and families desperately need rapid, effective treatments that target the core pathophysiology of serious mental illnesses and the tools for early detection. Mental illness research can develop new diagnostic markers and treatments, but this will require defining the pathophysiology of these illnesses.

NAMI also supports efforts at NIMH to translate basic research findings on brain function into more person-centered and multifaceted diagnoses and treatments for mental disorders. The Research Domain Criteria (RDoC) project is showing enormous promise toward efforts to build a classification system based more on underlying biological and basic behavioral mechanisms than on symptoms, RDoC should begin to give us the precision currently lacking with traditional diagnostic approaches to mental disorders.

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

NAMI is disappointed by the relative absence of innovative public-private partnerships and venture philanthropy focused on serious mental illness. While there is significant investment of private philanthropy on mental illness and suicide prevention research, these efforts tend to lack focus and coordination.

More importantly, NAMI has been frustrated by the lack of focus of burgeoning public-private partnerships on serious mental illness. NAMI was especially disappointed that the initial priorities undertaken by the Accelerating Medicines Partnership (AMP) between the NIH and the 10 largest pharmaceutical companies completely excluded serious mental illness, and that schizophrenia was actually dropped from a preliminary list of candidate disease states. AMP is a huge opportunity to develop and harness large scale collaborative efforts that can grapple with heterogeneous disease states and validate biomarkers in large patient populations. The removal of schizophrenia from the initial list of AMP priorities is a major disappointment. NIH and their industry partners must address this exclusion moving forward.

At the same time, NAMI does support President Obama's BRAIN Initiative (Brain Research through Advancing Innovative Neurotechnologies) and the request for a \$40 million increase for FY 2015, up to \$100 million. The BRAIN Initiative shows promise for a multi-agency collaboration with a number of foundations designed to unleash new technologies and undertake basic mapping of circuits and neurons in the most complex organ in the human body. NAMI is hopeful that it will yield tremendous advances in understanding the foundations and future of neurosciences. The BRAIN Initiative's three federal funding agencies, NIH, National Science Foundation (NSF) and Defense Advanced Research Projects Agency (DARPA), are already

collaborating with private organizations to leverage advances in nanoscience, imaging, engineering and informatics. The coordination of scientific advances to a common purpose – improving neurological research tools -- will accelerate the development of better diagnostics and treatments for brain ailments. NAMI urges the Committee to support this vital research program.

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

In NAMI's view, there is an urgent need for new medications to treat serious mental illness. Existing medications can be helpful, but they often have significant limitations; in some cases requiring weeks to take effect; failing to relieve symptoms in a significant proportion of patients; or, resulting in debilitating side effects. However, developing new medications is a lengthy and expensive process. Many promising compounds fail to prove effective in clinical testing after years of preliminary research. To address this urgent issue, NAMI is encouraging NIMH in working to accelerate the pace of drug discovery through an 'experimental medicine' approach to evaluate novel interventions for mental illnesses. This "fast-fail" strategy is designed not only to identify quickly candidates that merit more extensive testing, but also to identify targets in the brain for the development of additional candidate compounds. Through small trials focused on proof-of-concept experimental medicine paradigms, we can make progress to demonstrate target engagement, safety, and early signs of efficacy.

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

Over the years, NAMI has worked hard to develop strong alliances with major research institutions across the nation and the world --- in government, academia, private industry and philanthropy. These collaborations are now beginning to deliver promising results in for newer and more effective interventions, particularly with respect to early intervention in psychotic disorders. As many as 100,000 young Americans experience a first episode of psychosis (FEP) each year. The early phase of psychotic illness is a critical opportunity to alter the downward trajectory and social, academic, and vocational challenges associated with serious mental illnesses such as schizophrenia. The timing of treatment is critical; short- and long-term outcomes are better when individuals begin treatment close to the onset of psychosis. Unfortunately, the majority of people with mental illness experience significant delays to seeking care—up to two years in some cases. Such delays result in periods of increased risk for violence, especially suicide.

NIMH-funded research has focused on the prodrome, the high-risk period preceding the onset of the first psychotic episode of schizophrenia. Through North American Prodrome Longitudinal Study (NAPLS) and other studies focused on early prediction and prevention of psychosis, NIMH has launched Early Psychosis Prediction and Prevention (EP3) initiative. EP3 is showing promise in detecting risk states for first episode psychosis.

NAMI also supports efforts on the part of the federal government to advance "translational" research. The National Center for Advancing Translational Sciences (NCATS) is the newest of

27 Institutes and Centers (ICs) at the National Institutes of Health (NIH). This Center was established in December 2011 to catalyze innovative methods and technologies to enhance the development, testing, and implementation of diagnostics and therapeutics across a wide range of human illnesses. Among NCATS' important initiatives is the "Discovering New Therapeutic Uses for Existing Molecules" program. NCATS collaborated with four private pharmaceutical companies to make 26 therapeutic agents available to researchers to crowdsource ideas for new uses. NIH, working together with industry partners, can improve therapeutic development process and speed treatments to patients in need.

Both the BRAIN Initiative and NCATS are supported with from existing appropriations; not additional funding support. As important as the BRAIN Initiative and NCATS are to overcoming regulatory barriers; neither is a substitute for sustained, robust funding of biomedical research. NAMI urges the Committee's support to encourage Congressional appropriators to restore NIH's eroded purchasing power.

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

NAMI is proud of its longstanding collaboration with the NIMH. Our most recent collaboration with NIMH involved services intervention research. The NIMH Recovery After an Initial Schizophrenia Episode (RAISE) Project is aimed at preventing the long-term disability associated with schizophrenia by intervening at the earliest stages of illness. The RAISE Early Treatment Program (RAISE ETP) will conclude in 2014. The RAISE Connection Program has successfully integrated a comprehensive early intervention program for schizophrenia and related disorders into an existing medical care system. This implementation study is now evaluating strategies for reducing duration of untreated psychosis among persons with early-stage psychotic illness.

NAMI is also coordinating with NIMH on a research agenda to address early mortality in serious mental illness. When individuals with schizophrenia and bipolar disorder progress to later stages of their illness, they become more likely to develop—and die prematurely—from medical problems such as heart disease, diabetes, cancer, stroke, and pulmonary disease than members of the general population. NIMH funded research is demonstrating progress advancing the health of people with serious mental illness. NAMI supports efforts at NIMH to advance this research to large-scale clinical trials aimed at reducing premature mortality with people living with serious mental illness.

***How do you learn about new treatments and cures? How do you communicate with other patients regarding treatment and cures?***

NAMI collaborates closely with senior staff at NIMH and in academia to access and disseminate the latest scientific findings. This includes regular meetings with the leadership at NIMH and participation in the semi-annual NIMH Alliance for Research Progress meetings. In addition, NIMH Director Tom Insel regularly presents at our annual convention. Finally, we also use broad range of publications and on-line tools to share research results with our membership of people living with mental illness and their families.

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

NAMI is supportive of the risk-benefit framework that was included in the FDA Safety and Innovation Act of 2012 (FDASIA, P.L. 112-144). These changes were an important step forward in bringing greater transparency to the benefit-risk assessments at the FDA. Prior to FDASIA, the interests of patients and their families were not taken into account makes that too many of us has often been opaque and difficult to understand, especially when decisions have been made across multiple divisions and offices. The improvements in this Agreement should bring more transparency to this process. Increasing the public's understanding of this process should also help improve public confidence in the agency's decisions.

NAMI is pleased that FDASIA and the PDUFA V Agreement are already bringing greater transparency to the benefit-risk assessments FDA makes that too many of us has often been opaque and difficult to understand, especially when decisions have been made across multiple divisions and offices. The improvements in this Agreement should bring more transparency to this process. Increasing the public's understanding of this process should also help improve public confidence in the agency's decisions.

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

Both public and private investments in scientific research aimed at developing newer and more effective treatments are critical. Each has unique and complimentary roles – the NIH in basic scientific, translational and services research and private industry in developing and bringing to market both breakthrough therapies and incremental improvements that can improve adherence and respond the complex needs of individual patients. The new challenge new is that the severe constraints placed on federal discretionary spending in recent years – changes likely to stay in place over the coming decade – are likely to keep funding at the NIH flat or below the cost of research inflation.

On the private industry side we have seen more and more companies pull back from investments in neuroscience research in recent years. This is occurring as a result of the high failure rate that too often occurs in clinical trials involving not only serious mental illness, but across all of neuroscience. We know that the brain is the most complex human organ. Molecular targets are elusive and there are few animal models to assist in development of biomarkers.

At the same time, there are promising developments on the horizon. New genomic technologies, combined with global collaborations are showing promise in identifying and growing number alleles associated with schizophrenia and bipolar disorder. Molecular pathways involved in neuronal function are emerging and beginning to suggest valid drug targets. Animal and in vitro models in which to investigate hundreds of gene variants of small effect are still elusive. However, promising tools are emerging here as well. When combined with new genome engineering tools, these approaches permit the study of individual risk alleles, multiple alleles in molecular pathways, and the correction risk alleles in neurons derived from patient samples.

NAMI is hopeful that the early stages of the successful Alzheimers Disease Neuroimaging Initiative can serve as a model to identify new biomarkers in schizophrenia.

It is critical for NIH and industry to use AMP as a tool to foster greater collaboration to jumpstart these opportunities for development of new treatments.

***How can Congress help?***

NAMI urges Congress to move forward on legislation to better align incentives for drug discovery and promote development of new therapies and diagnostics. In particular, NAMI urges Congress to pass the MODDERN Cures Act (HR 3116), sponsored by Representative Leonard Lance of New Jersey. HR 3116 would update the current drug evaluation process to encourage the discovery and development of new treatments for chronic and rare diseases. It would also provide a pathway to bring promising new compounds to market and establish a predictable timeline for the introduction of generic equivalents. In addition, it advances creative solutions for developing companion diagnostic tests and create a system that rewards efficiency and effectiveness to the benefit of people living with serious and disabling illnesses, including serious mental illnesses such as schizophrenia and bipolar disorder.

NAMI also supports the Youth Mental Health Research Act (HR 4170), authored by Representative Chaka Fattah of Pennsylvania. By authorizing a Youth Mental Health Research Network at the NIH, HR 4170 would advance mental illness research and ensure better focus on early detection, greater coordination of multisite clinical trials of available early intervention therapies and more rapid dissemination of scientific findings resulting from such trials. This will promote greater replication and adherence to the guidelines, protocols, and practices developed and validated in important studies on early intervention in psychosis such as the North American Prodrome Longitudinal Study (NAPLS) and the Recovery After an Initial Schizophrenia Episode (RAISE) study. NAMI urges the Committee to support HR 4170.

Respectfully Submitted,

Mary Giliberti, J.D., Executive Director  
National Alliance on Mental Illness

June 16, 2014



National  
Multiple Sclerosis  
Society

June 12, 2014  
The Honorable Fred Upton  
The Honorable Dianna DeGette  
2125 Rayburn House Office Building  
Washington, DC 20515

## RE: The 21<sup>st</sup> Century Cures Initiative

The National Multiple Sclerosis Society (Society) applauds the Energy and Commerce (E/C) committee, particularly Chairman Upton and Congresswoman DeGette, for their leadership and commitment to this thoughtful initiative. We are grateful for the opportunity to provide feedback in a multitude of formats for this initiative. In addition to providing these comments, E/C staff also attended a meeting of high-level research advisors to the Society on June 12. A summary of that discussion is included in our comments below.

Multiple sclerosis (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.

The National MS Society sees itself as a partner to the government in many critical areas. While we're here to advocate for governments involvement in accelerating the discovery, development and delivery of new treatments, we do it as an organization that commits nearly \$50 million annually in MS research through funds generated by the Society's fundraising. Since our inception, we have funded \$820 million in MS research. Our goal is to see a day when MS has been stopped, lost functions have been restored, and a cure is at hand.

The Committee has asked how to incentivize, leverage, and harness our nation's abilities to develop new solutions to our most pressing health care needs. The following comments offer recommendations and ideas to advance that goal, but this should not be considered an exhaustive list of all the possibilities.

### Background on MS

#### Financial Burden of Disease

The average annual costs for someone with MS in the U.S., including both direct and indirect costs (i.e. lost wages), is approximately \$69,000. Of this, approximately \$39,000 consists of health care costs. When you extrapolate this cost to the estimated MS population of ~400,000, the total costs for all people with MS in the U.S. is approximately \$28 billion annually. These costs escalate as disability increases and the need for greater assistance is needed. People living with a more disabling form of the disease usually incur about twice as many costs than those living with a milder form of MS.



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Due to the financial burden, 25% people living with MS have individual incomes that fall below the federal poverty level. Progression and severity of the disease is a big predictor on the impact on finances. People with a more aggressive form of MS, primary progressive MS, are more likely to be unemployed (82% unemployed) when compared to those with relapsing-remitting MS (42% unemployed), a less aggressive form of MS.

### State of the Treatments in MS

Currently, there are 13 therapies specifically designated to treat and manage MS. Of those treatments, 10 are disease modifying drugs that are shown to modify the course of MS in relapsing-remitting MS. While the development of these treatments has been a tremendous achievement, each therapy only works for a subset of patients and none of them are indicated for progressive forms of MS.

In order to address the unmet needs of people living with progressive MS, the National MS Society has partnered with other international groups to form the International Progressive MS Alliance. This group is charged with creating a network of resources and experts to develop systems and solutions to treat progressive MS. Outside of this work, large-scale trials are also underway to examine whether certain existing and new treatments might have an effect on progressive MS.

In addition to traditional pharmaceutical treatments, wellness initiatives are another way people with MS try to treat and manage their disease. While there is anecdotal information about the benefit of diet and exercise, additional research is needed to determine which programs are the most effective for the overall health of someone living with MS. People with MS report that many wellness programs not only maintain functioning and movement but also help with the psychological factors of MS, by connecting them to a broader community. Therefore, we would encourage you not only to focus your work on how to advance the development of pharmaceuticals and devices but also dedicate resources to understanding the value of wellness programs for chronic neurological conditions, like MS.

### Existing Programs to Support/Foster Research

The Society dedicates considerable funding to traditional research streams, such as basic research and clinical trials. In addition to supporting clinical trials financially, the Society also acts as a repository of information for patients interested in participating in clinical trials. The Society's website ([www.nationalmssociety.org](http://www.nationalmssociety.org)) publishes all the opportunities to participate in clinical trials, surveys, tissue banks and genetic analyses. Individuals can also sign up for alerts when new clinical trial opportunities become available. This information helps to facilitate clinical trial recruitment.

However, the Society has found that getting treatments to patients involves more than funding basic research and that investment at every stage of the research process is needed. Often, the biggest hurdle in moving potential treatments forward is securing the necessary early investments and resources for commercial development - when the potential return of those investments is largely unknown. Yet, without this commercial development, solutions remain outside our grasp.

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The Society continues to accelerate promising new therapies and diagnostics by breaking down barriers to commercial development through our venture philanthropy, Fast Forward. We make connections between a diverse set of stakeholders needed to ensure that promising treatments continue through the drug development pathway. As an important part of the Society's research infrastructure, investments through Fast Forward continue to bring new companies to address unmet needs in MS and promote the transition of these innovative approaches to subsequent steps in clinical development. The Society will continue to work diligently to close the gap between promising discoveries and the commercial development necessary to get new treatments to people with MS.

## Discovery

### Accelerating Basic Research

There are three components needed to accelerate basic research in MS—1) consistent funding 2) more timely demographic data 3) better coordination both within the government agencies and with external partners.

In order to incentivize researchers to go into the field, more predictable funding for the National Institutes of Health (NIH) and other streams, such as the Congressionally Directed Medical Research Programs (CDMRPs) need to be committed. Researchers need a steady source of funding to conduct continuous research and assure young scientists of a career path. The Committee's white paper identifies the importance of federal funding of the basic research that begins and underpins the process of discovery. The importance of having a sustained commitment to funding basic research cannot be overstated. Congress must focus on how to increase the NIH/CDMRP budget appropriately on an annual basis. Without such an annual increase, the budget and nation's ability to fund meritorious research effectively and at a level that advances innovation declines with the inevitable increases in the cost of research.

In addition to funding these public agencies, Congress should also encourage better priority setting and coordination of medical research. At present, there is very limited coordination among NIH institutes, the Department of Defense and the National Science Foundation. Duplication of effort and lack of direction plague medical research. Federal support of medical research needs to be more rationally directed toward clear goals and objectives. This also applies to private funders. The government should work to coordinate with foundations and private firms, which will help to address areas of need that are not being met by public funding.

Another barrier to accelerating MS basic research is the data on the incidence and prevalence of MS are vastly outdated. The last government study that was done was conducted in 1975. Over the past 7 years, the Society has worked to try to pass a bill establishing a neurological registry (also called the surveillance system). Establishing this sort of database would be extremely helpful in determining patterns and potential triggers for MS, in addition to better understanding the number of people living with MS in the United States. If Congress wants to accelerate research, they need to dedicate resources to tracking prevalence data.



## Development

### Translational Science

With the development of the National Center to Advance Translational Sciences (NCATS) at the NIH, the government has committed both resources and funding to explore the repurposing of existing drugs for other diseases. While we applaud this effort and see that there could be a direct benefit for people living with MS, we are concerned that there is not currently the incentives/mechanisms to entice a company to seek another indication, especially for drugs where the patent has already expired. The Society would encourage Congress to look at a means to fund not only Phase II trials but also Phase III trials through NCATS, or look at alternative financial models to encourage a complete study of these agents.

### Clinical Trials

In regards to accelerating clinical trials, the MS community has noted two issues related to clinical trials—finding ways to encourage data sharing and international coordination in small subpopulations of patients.

The first area that the Society believes could be improved is modifying the current protections around intellectual property for drugs. Currently, the Society is engaged with a number of pharmaceutical companies, the Food and Drug Administration (FDA) and the Critical Path Institute in an effort to devise a new clinical trial outcome measure for MS. Through this process, we have encountered reluctance by some researchers to share their data because of the lack of protection for their intellectual property, even though the result would be achieving a common goal of speed and sensitivity of clinical trials. Researchers need to be assured their intellectual property will be protected, in order to innovate and accelerate the clinical trials process, which Congress could help address.

Additionally, international coordination of clinical trials and agreement with other regulatory agencies is especially important for small subsets of patients, like those living with pediatric MS. Estimates suggest that 8,000-10,000 children (up to 18 years old) in the United States have MS, and another 10,000-15,000 have experienced at least one symptom suggestive of MS. Given both the small size of the group and the unique characteristics of children, recruitment for pediatric MS trials is difficult and fewer studies can be conducted. Therefore, it is imperative in order for these clinical trials to succeed that there is an agreement between the FDA and other international regulatory agencies about clinical trial design and acceptable outcome measures.

### Aligning incentives

While the MS research community is proud of the development of 10 disease modifying therapies in the past 20 years, MS is not cured and for many there are still no treatments available to help slow the progression of their disease. The current therapies on the market are aimed at stopping progression for those with MS; however, MS researchers are still looking for ways to restore function and the possibility to end the disease forever. The progressive form of MS is one area where we have no approved



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treatments and people living with this type of MS often experience the biggest impact in terms of disability and financial burden. While part of the puzzle to treat progressive MS lies in lack of scientific understanding, there are also fewer incentives for companies to invest in researching a treatment for progressive MS. While most people diagnosed with relapsing-remitting MS eventually transition to a progressive form of the disease, only 10% of the MS population is initially diagnosed with primary progressive MS. Because progression can be slow, it can take a long time for a pharmaceutical company to study whether an agent is working. Additionally, since MS is a disease of the central nervous system, it is more difficult to study. Therefore, due to the increased time and resources needed to study treatments for progressive MS, many companies may not choose to invest in this because of the potential lack of return-on-investment.

### Evaluating Benefit-Risk in Treatments

The benefit-risk paradigm is of particular interest to the MS community. There is generally a range of risk tolerance within the group and often individual patients' tolerance for risk changes over time. Progression, life stage and previous treatments all impact risk tolerance in a patient. Regulators need to do a better job of supporting and encouraging research to understand and document how risk tolerance changes, in order to create an appropriate risk environment, which will permit patients and physicians to comfortably weigh risk-benefit in the face of adequate information concerning both. In order to address this issue, Congress could mandate that the FDA recommend ways to appropriately gather benefit-risk information from patient populations.

### Delivery

#### Affordability

Better treatments can help only if they are affordable. At present, the benefits of MS treatment on quality of life and disability are modest in comparison to the costs of achieving those benefits. Treatments with an improved cost-benefit profile would save money by allowing people to remain employed longer, reduce burden on caregivers, and reduce health care costs. Currently, this equation is not as favorable as it could be, owing to the high cost of MS drugs. Therefore, Congress should develop incentives for accelerating treatments that do not encourage the further escalation of prices.

Thank you again for your leadership in this area and we look forward to working with you on this initiative moving forward. If you need any assistance from our organization, please do not hesitate to contact me ( [REDACTED] ) or Lauren Chiarello, Senior Director of Federal Government Relations [REDACTED]

Sincerely,

[REDACTED]

Bari Talente  
Executive Vice President, Advocacy  
National Multiple Sclerosis Society

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June 13, 2014

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

Dear Chairman Upton,

On behalf of the 30 million men, women, and children affected by one of the nearly 7,000 known rare diseases, the National Organization for Rare Disorders (NORD) thanks Chairman Upton and the Energy & Commerce Committee for their continuing support of the rare disease community. We are excited to participate in the 21<sup>st</sup> Century Cures Initiative, a bi-partisan effort within the House Committee on Energy & Commerce aimed at improving the treatment discovery, development, and delivery process in the United States.

NORD is a unique federation of voluntary health organizations dedicated to helping people with rare "orphan" diseases and assisting the organizations that serve them. NORD is committed to the identification, treatment, and cure of rare disorders through programs of education, advocacy, research, and patient services.

We welcome the opportunity to comment on the 21<sup>st</sup> Century Cures Initiative's third white paper titled, "Patients". This white paper poses the question of how we can close the gap between the number of diseases and the number of treatments. Obviously, this is an extremely important topic for NORD, as the vast majority of diseases without a treatment are rare.

In order to address this question, we have developed the following proposals to accelerate the pace of medical innovation, and ensure that all rare disease patients receive the treatment they deserve. We look forward to discussing these ideas with the Energy & Commerce Committee as the 21<sup>st</sup> Century Cures Initiative continues.

### **1. Ensure Sufficient and Consistent Funding for the National Institutes of Health (NIH)**

To assure that the basic, translational and clinical research system remains strong in the United States, Congress must provide sufficient and consistent funding for the NIH. The NIH is currently vastly underfunded, as yearly appropriations have largely remained stagnant since

2005. The recently proposed funding level for the NIH in the FY 2014 budget is actually lower than what the NIH received in 2012.<sup>1</sup>

Not only is the NIH sorely underfunded, but the cyclical unpredictability of NIH funding is detrimental to medical research. Funding interruptions or alterations can derail projects, resulting in the loss of potentially valuable medical research. This also turns promising early career investigators away from research careers, a problem that then has long-lasting effects on the next generations of researchers.

The NIH operates several programs and initiatives that are critical to rare disease research. The National Center for Advancing Translational Sciences (NCATS) conducts various initiatives that advance innovation in rare disease research. NCATS collaborates with industry partners and academia to find new therapeutic uses for existing molecules, many of which may be effective in treating rare diseases.<sup>2</sup>

NCATS operates the Clinical and Translational Science Awards (CTSA) program which funds and coordinates clinical and translational research in over sixty research institutions across the United States.<sup>3</sup> NCATS also operates the Therapeutics for Rare and Neglected Diseases (TRND) program which collaborates with academic researchers, patient organizations, and industry to speed the development of therapies for rare diseases.<sup>4</sup>

Finally, the Office of Rare Diseases Research (ORDR) within NCATS supports the Rare Diseases Clinical Research Network (RDCRN) and operates a rare disease database with nearly 7,000 diseases included.<sup>5</sup>

If the 21<sup>st</sup> Century Cures Initiative is to succeed in strengthening the medical research framework of this country, it must strengthen NIH funding and then remove the unpredictability of funding levels each year.

## **2. Create Incentives for Researchers to Enter the Rare Disease Research Field**

Funding the NIH at an appropriate level will be effective in accelerating the pathway to cures only if we have talented and well-trained researchers to conduct the research. As proposed in NORD's previous 21<sup>st</sup> Century Cures Initiative Comments, Congress should create incentives to medical professionals in training for entering the rare disease field.

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<sup>1</sup> Johnson, Judith A. "Brief History of NIH Funding: Fact Sheet" *Congressional Research Service*, 23 Dec. 2013 Web. 13 June 2014

<sup>2</sup> "Discovering New Therapeutic Uses for Existing Molecules" *National Center for Advancing Translational Sciences*, May 2014 Web. 13 June 2014

<sup>3</sup> "About the CTSA Consortium" *Clinical Translational Science Awards*, Web. 13 June 2014

<sup>4</sup> "Therapeutics for Rare and Neglected Diseases" *National Center for Advancing Translational Sciences*, Web. 13 June 2014

<sup>5</sup> "The Rare Diseases Clinical Research Network" *Office of Rare Diseases Research*, Web. 13 June 2014

Within the NIH, Congress could create incentives, such as further fellowship funding or student loan repayment for entering rare disease research. Not only will this accelerate the pace of rare disease research, it will also accelerate innovations in treating common diseases, as many medical breakthroughs for common diseases originated with research into rare diseases.

Finally, with targeted incentive programs, Congress can assist in supporting early career rare disease research investigators by encouraging NIH to enlarge the presence of clinical investigator expertise, and the science of small clinical trials, throughout its grant review process.

By expanding the pool of researchers who focus on rare diseases, Congress will accelerate the pace of medical discovery for both rare and common diseases.

### **3. Commission a “National Plan for Rare Diseases”**

The U.S. needs a consensus document that sets for a National Plan for Rare Diseases. This agenda would address many of the questions that the “Patients” white paper asks.

First, Congress should examine the Institute of Medicine’s (IOM) 2010 report titled “Rare Diseases and Orphan Products: Accelerating Research and Development”.<sup>6</sup> This report aims to implement an overarching national strategy for rare disease research and product development.

After examining existing recommendations on how to improve the nation’s rare disease research system, Congress should commission a comprehensive agenda that evaluates the entire rare disease healthcare ecosystem, and makes recommendations on how to improve the discovery, development, and delivery of treatments to rare disease patients. Congress can follow the precedent of other National Plans it has commissioned, such as the National Plan to Address Alzheimer’s.<sup>7</sup>

This plan must be entirely comprehensive and cover the entire spectrum of the rare disease landscape. It should address the duties of each public agency involved in rare disease treatment discovery, development, and delivery. This plan must also address how these public agencies can collaborate with private entities to improve the rare disease ecosystem.

Within this National Plan, Congress should specifically commission the following:

- **National Rare Disease Research Recommendations**

Congress can strengthen the basic and translational rare disease research ecosystem by requesting the Orphan Products Board (see NORD’s comments on the 21<sup>st</sup> Century Cures’ first white paper) to publish a yearly agenda with recommendations for rare disease research and products development.

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<sup>6</sup> “Rare Diseases and Orphan Products” Institute of Medicine, Oct. 2010, Web. 13 June 2014

<sup>7</sup> “National Plan to Address Alzheimer’s Disease: 2014 Update” U.S. Department of Health & Human Services Web. 13 June 2014, <<http://aspe.hhs.gov/daltcp/napa/NatlPlan2013.shtml>>

The Orphan Products Board will work, in consultation with the NIH and FDA, to recommend advances in innovative clinical trial designs for orphan therapies. The Orphan Products Board will also work with the Centers for Disease Control and Prevention (CDC) on epidemiological techniques and advances.

In developing this agenda, the Orphan Products Board will consult with government, medical, and academic researchers. The Orphan Products Board will also consult with sponsors on how to facilitate bringing products to market. Finally, the Orphan Products Board will consult with patients on priorities in developing new treatments.

- **The Benefits of Rare Disease Research on the Economy and Healthcare System**

Rare diseases are generally costlier to treat, per capita, than more common diseases, because rare diseases often take between five and ten years to diagnose, orphan therapies are often more expensive, and the vast majority of rare diseases are chronic, thus leading to a life-time of healthcare costs.

As part of this National Plan, Congress should commission a study on how better funding and coordination of rare disease research will benefit the economy and the healthcare system, as well as lower the Federal government's healthcare expenditures. Greater coordination of research will foster a more efficient use of public and private resources.

- **National Agenda on Rare Disease Registries and Natural History Studies**

Natural history studies and registries play a critical role in the drug discovery and development process. Patient registries represent one of the best resources to collect prevalence, demographic, natural history, and comparative effectiveness data on rare diseases. Standardized natural history registries, tied to tissue banking, facilitate the generation of research leads, and accelerate studies examining associations between phenotype (disease-related physical and mental characteristics) and genotype. Currently, very few rare disease patient registries exist and where they do, they are often limited in their usefulness.

In collaboration with the NIH and FDA, NORD is currently in the process of building a rare disease patient registry program to ensure rare disease patients have adequate natural history information in order to spur drug discovery and development.

We cannot do it alone, however, and with nearly 7000 diseases without a treatment, Congress should commission a plan to coordinate rare disease patient registries and

natural history studies in order to catalyze drug discovery and development for these diseases.

- **National Agenda for the Collection of Rare Disease Data**

While there have been great advancements in our collective knowledge on rare diseases, there is still far much more we need to learn in order to find treatments and cures for the nearly 7,000 diseases with no treatment.

Congress can start to address this knowledge gap by mandating that rare disease information, including prevalence, length of diagnosis, off-label prescription use, and many others, be included within the already existing data collection efforts undertaken by various government agencies. With this information, we will better understand the challenges facing the rare disease patient, and will be better able to address these challenges.

**4. Ensure All Current Laws that Increase the Patient's Involvement are Implemented Fully**

While NORD believes that the patient's voice must be strengthened in the drug development and approval process (see #5), we first need to assure that current laws addressing patient involvement are being implemented fully. The Food and Drug Administration Safety and Innovation Act (FDASIA) made groundbreaking strides in encouraging that patients play a greater role during the drug approval process. The FDA has implemented many of these changes admirably but there are various other measures contained within FDASIA that are not being implemented to the fullest extent, or not at all.

First, the FDA must include a patient or patient representative on the drug review committee as mandated by section 903 of FDASIA.<sup>8</sup> While the FDA has increased patient involvement in other aspects of the drug approval process, such as in Advisory Committee Hearings, the FDA has yet to include patients on a review panel. The FDA should be required to fulfill this mandate.

Second, while the FDA has conducted several patient-focused drug development meetings, it has yet to demonstrate how it intends to use the collected information to inform the drug review process. While NORD appreciates the FDA's efforts in implementing the patient-focused drug development initiative, we are particularly eager for the findings from these meetings to be incorporated within the drug review process.

Finally, NORD requests that the FDA develop a guidance advising patient organizations on how they can administer their own patient-focused drug development meetings and provide data that

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<sup>8</sup> Food and Drug Administration Safety and Innovation Act § 903

will be useful to the drug approval process. Under current law, the FDA is to hold twenty patient-focused drug development meetings. The information derived from these meetings can be broadened substantially if FDA provides guidance on how patient organizations can independently conduct their own patient-focused drug development meetings in a manner that would enable the FDA to use the findings of these meetings to enhance the drug review process.

## **5. Expand Patient Partnerships Within the FDA**

We advocate that patients be regarded and treated as partners with the FDA in the drug review process. At present, despite progress, patients are regarded as outside participants who are asked to occasionally consult on drug efficacy and effectiveness, usually under the auspices of the drug companies.

We urge FDA to standardize patient input within the drug review process. Currently, the level of patient involvement varies among review divisions. Patient contribution at regular and predictable times must be built into the process.

Rare disease patients, their families, and their caregivers can be most useful for the FDA when assessing the benefit-risk of a therapy. In its “Patients” white paper, the 21<sup>st</sup> Century Cures Initiative asks, “How should regulators evaluate benefit-risk? How do you work with regulators regarding benefit-risk? Can this process be improved?”

It is NORD’s opinion that patients can make significant contributions in helping to evaluate the benefit-risk of a drug. Patients must be equal partners with the FDA and companies in making this assessment.

## **6. Ensure Sufficient and Consistent Funding for the Food and Drug Administration**

Much like the NIH, the FDA is also drastically underfunded for the wide array of regulatory responsibilities it maintains. The FDA is continually charged by Congress with additional oversight responsibilities, not to mention the drastic expansion of existing responsibilities due to globalization and increasingly diverse scientific innovations.

It is NORD’s belief that the FDA desires to undertake and complete many, if not all, of the reforms NORD has called for within our responses to the 21<sup>st</sup> Century Cures White Papers. However, they simply do not have the means to do so.

It is time for Congress to recognize the importance of the FDA and dramatically increase the yearly appropriations the FDA receives. The 21<sup>st</sup> Century Cures Initiative can accelerate the pace at which treatments reach the patient by giving the FDA the resources they need to utilize the expedited review pathways for all treatments that qualify. Appropriate funding will also allow the FDA to ensure its review staff is well trained in the newest scientific breakthroughs, and will allow them to engage the patient community at every opportunity.

## **7. Ensure Reimbursement for “Non-Conventional” Rare Disease Therapies**

In NORD’s comments on the 21<sup>st</sup> Century Cures Initiative white paper titled, “A Call to Action”, we highlight the issue of high cost-sharing within drug formularies for specialty drugs, many of which treat rare diseases. We also discuss off-label reimbursement issues, and the importance of off-label use of therapies for rare disease patients.

These are several of many reimbursement issues facing patients with rare diseases, including lack of coverage of orphan therapies under the Medicare and state Medicaid programs.

While reimbursement problems exist for all orphan therapies, we are particularly concerned about issues surrounding “non-conventional” treatments, especially the lack of reimbursement for such products.

For the purposes of this paper, NORD defines non-conventional therapies as treatments that are not the standard “small-molecule” drug or “large-molecule” biologic. Instead, “non-conventional” therapies are treatments such as medical foods for Inborn Errors of Metabolism (as well as various other rare diseases), medical devices (particularly humanitarian use devices), bio-engineered treatments, and more.

NORD is concerned that the reimbursement model that the Federal, State, and private health insurance plans utilize often ignores the importance of these therapies, and how critical they are to the survival of many rare disease patients. As Congress addresses the discovery, development, and delivery of treatments for rare disease patients, NORD requests that Congress stay particularly mindful of diseases that require therapies, such as medical foods and humanitarian use devices that do not fall within the common categories of drugs and biologics.

Thank you again for the opportunity to engage in this exciting and much-needed initiative. We look forward to working with Chairman Upton and the Energy & Commerce Committee as the 21<sup>st</sup> Century Cures Initiative continues, and we are grateful for the Chairman’s recognition of these extremely important issues within the rare disease community.

For questions regarding NORD or the above comments, please contact Diane Dorman, Vice President of Public Policy, at [REDACTED].

Sincerely,

[REDACTED]

Peter L. Saltonstall  
NORD President and CEO



Mission: To find a cure for psoriasis and psoriatic arthritis  
and to eliminate their devastating effects through research, advocacy and education.

June 13, 2014

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

Re: 21<sup>st</sup> Century Cures Initiative

Dear Chairman Upton and Ranking Member Waxman:

On behalf of 7.5 million Americans living with psoriasis and psoriatic arthritis –our nation’s most common autoimmune disease – we are writing to commend you for undertaking the 21<sup>st</sup> Century Cures Initiative. Such a comprehensive examination of what we are doing – in the public and private sectors – to develop cures and therapies for our most debilitating diseases and conditions, is much needed. While Congress, particularly your committee, has done much work in this space over the years, including NIH Reform and the various user fee laws, these efforts have often been soiled in a way that prevents a full exploration of their many interconnected components. Hopefully, the 21<sup>st</sup> Century Cures process will permit a more complete review of what is working and help identify gaps or challenges to address.

The National Psoriasis Foundation is the largest psoriasis patient advocacy organization and charitable funder of psoriatic disease research worldwide, assisting approximately 1.5 million people annually through educational programs and services. We are relentless in our mission to find a cure for psoriasis and psoriatic arthritis and to eliminate the devastating effects of this disease. Psoriasis and psoriatic arthritis are chronic, inflammatory, painful and disfiguring autoimmune disease for which there are limited treatment options and no cure. Recent studies have found that people with psoriasis are at elevated risk for other chronic and debilitating health conditions such as heart attack, diabetes, obesity, and other diseases. Additionally, people with severe psoriasis have a 50 percent higher risk of premature death. Access to treatment is important to prevent much of the disability and psychosocial impacts of the disease.

Thankfully, our community is fortunate to have a number of treatments for psoriasis and psoriatic arthritis including topicals, phototherapy or light treatment and a number of drugs and biologics. While there is no cure for psoriasis or psoriatic arthritis, many patients are able to effectively manage their illness using one or more of these therapies. This is still not enough. Given the nature of the disease, a treatment that may result in near or total clearance of the disease for one patient may have modest to no impact for another. Additionally, it is not uncommon for our patients to have to alter their course of therapy over their lifetime after a medication’s efficacy diminishes.

Another major concern for our community is access to the treatments deemed necessary by their physicians. Access barriers include high copays for phototherapy treatment regimens that deter use of this treatment medium, even though such treatment could help delay or minimize the use of biopharmaceutical treatments, which come with greater side effects and higher costs. Another significant barrier is that of high out-of-pocket costs for drugs given that many of the treatments for our community are biologics or specialty drugs. Cost are not considered until treatments have been approved, low-cost treatments would benefit our patient community. Recent actions by pharmacy benefit managers and similar entities have restricted access to some specialty drugs. While we understand that the bulk of the Cures Initiative is focused on research and development issues, we would urge the committee to not neglect access and to promote a robust dialogue and conversation on this topic.

NPF has reviewed your patient-oriented white paper issued on May 16<sup>th</sup> and the many questions you have posed in that document. Following are responses from NPF to a subset of those questions.

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

As mentioned above, we are fortunate to have a number of treatments options today along with a robust pipeline with about 40 candidate treatments – drugs, injectables and topicals – in various stages of clinical evaluation.<sup>1</sup> At the same, as also noted above, there is no cure for psoriasis and psoriatic arthritis and patient response to treatments varies widely. Building upon the comments in the introduction, patients with psoriasis and psoriatic arthritis are adversely affected by out-of-pocket costs, which continue to rise at unprecedented levels. Many insurers and pharmacy benefits managers place specialty drugs used to treat psoriatic diseases into their drug formulary category requiring the highest level of copayments. Additionally, late last year we saw PBMs move to tighten access further by proposing to exclude numerous specialty drugs altogether from their formulary, including drugs used to treat patients with psoriatic disease. While the policy was eventually amended, the final version still places such treatments in a high-cost tier, increasing patient copayments and, for an increasing number of patients, placing the treatment out of reach. From NPF's recent survey panel – 40 percent say cost is an issue in accessing treatment. Despite having insurance the majority of psoriasis and psoriatic arthritis patients pay more than \$2,500 in out-of-pocket costs per year; copayments for biologic drugs for psoriasis cost an average of \$1,500 per year; and one-third of patients say it's a financial strain to pay for their biologic drug.

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

Congress can help support efforts to more fully understand diseases like psoriasis and psoriatic arthritis. The epidemiology of psoriasis and psoriatic arthritis in the U.S. is poorly

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<sup>1</sup> See: <http://www.psoriasis.org/research/drugs-in-development/pipeline>

understood. We do not yet understand the natural history of the diseases, how it affects various populations differently, and how treatments impact disease progression. We are only just beginning to understand the relationship between psoriasis and other chronic conditions like diabetes and heart disease, and we do not understand how factors such as age or gender impact the course and burden of psoriasis and how certain environmental exposures might contribute to the occurrence and severity of psoriasis and psoriatic morbidities. Last year, the Centers for Disease Control and Prevention (CDC) released the Public Health Agenda for Psoriasis and Psoriatic Arthritis which enumerated many of the data gaps and other needs in the field. Developed through support provided by Congress, the agenda can serve as a roadmap for future research if properly supported going forward.

In addition to supporting public health data gathering, we also encourage ways to foster dialogue and in-depth collaboration involving patients, researchers and scientists from a number of disease fields, including those who have not focused extensively in a certain field but whose research may prove applicable.

Beyond adequately supporting public health and basic research efforts, Congress must look at ways to further accelerate the development of treatments and cures. The work of the recently established National Center for Advancing Translational Sciences (NCATS) and its Accelerating Medicines Partnership (AMP) are examples of public-private partnerships intended to reduce the time, the cost and the risk of therapy development. Reducing barriers that hinder clinical trial enrollment and execution, driving earlier access to data so drugs “fail faster” and forming early-stage collaborations to accelerate the pace of discovery are all valuable undertakings that, if successful, have the potential to reduce time and cost from the process. Doing so should, ultimately, help reduce the costs of novel therapies so they are more affordable and accessible.

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

Similar to the points above, Congress can continue supporting programs like NCATS and AMP intended to speed development of therapies. Later in the process, Congress should look to some of the reforms included in the September 2012 report of the President’s Council of Advisors on Science and Technology (PCAST), particularly those focused on reforming the clinical trials process so they keep pace with the evolution of science in the 21<sup>st</sup> century. More dynamic or adaptive trials that can be conducted using less time and resources yet while still obtaining necessary safety and effectiveness data along with greater alignment or harmonization with standards of regulatory authorities in other developed nations and regions, entities like the EMA, could be particularly helpful in accelerating breakthroughs into treatments and therapies.

### **4. What is the financial burden of your diseases? How would better treatments and cures help save money for your family and the federal government?**

Phototherapy (ultraviolet light therapy) is a first-line treatment for psoriasis. Phototherapy is also a critical treatment option for psoriasis patients who are prevented from taking other medications

because of conditions such as pregnancy, infection or malignancy or for patients whose immune systems are suppressed and who are not candidates for treatment by biologics. Phototherapy can be used in tandem with other medications, but in some cases it can delay use of biologics

Though phototherapy is relative inexpensive, the primary cost barriers to the treatment are the disproportionate copayments required by insurance companies as well as recent and potentially future cuts in Medicare reimbursement to physicians delivering such treatment in their offices. Many patients now face copayments as high as \$50 for one phototherapy visit. With a typical treatment regimen consist of 2 to 3 visits over 6 to 8 week period, out-of-pocket costs quickly soar and can be as much as \$600 for one month of treatment. In addition to helping produce better patient outcomes, phototherapy can actually help reduce or lessen the use of other treatments, particularly biologics that in total are far more costly. However, given the nature of our system, it is not uncommon for patients to pay less out-of-pocket for biologics than they would for phototherapy, helping drive total spending beyond what it may need to be.

Patients cannot be expected to pay larger and larger portions of the cost involved in order to access phototherapy, and providers cannot be expected to maintain a service for which utilization is decreasing.

In addition to phototherapy, as noted above, our community is facing higher payments for biologic medications to treat the disease. Given mounting concerns of the costs of novel drugs in other therapeutic areas and actions undertaken in 2013 to restrict access to certain specialty drugs, we anticipate such challenges will continue in the years ahead. The Avalere study examined 123 formularies from silver-level exchange plans — the benchmark plan that will generally pay 70 percent of covered medical expenses, leaving the consumer responsible for 30 percent – and found that a fifth of them required cost sharing of 40 percent or more for certain classes of specialty drugs used to treat psoriasis and psoriasis arthritis and other illnesses.<sup>2</sup> Avalere also concluded that 60 percent of silver plan formularies placed all medications for multiple sclerosis, cancer and other illnesses in the plan's highest formulary tier. That means patients who need these medicines would face the highest coinsurance percentage.

### **Conclusion**

Once again, on behalf of all Americans with psoriasis and psoriatic arthritis, we thank you for your leadership on 21<sup>st</sup> Century Cures and for reviewing our comments and recommendations. NPF is excited about where this initiative is going, and we stand ready to work with the Committee and the members on this important effort. If you have any questions about these comments, please contact Mr. Quardricos Driskell, NPF's Health Policy Manager at [REDACTED]

[REDACTED] Thank you in advance for your consideration. We look forward to working with you.

Sincerely,

Leah McCormick Howard, J.D.  
Director, Government Relations and Advocacy

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<sup>2</sup> See: <http://www.phrma.org/affordable-care-act/coverage-without-access-an-analysis-of-exchange-plan-benefits-for-certain-medicines>



Mission: To find a cure for psoriasis and psoriatic arthritis and to eliminate their devastating effects through research, advocacy and education.

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June 13, 2014

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

Dear Chairman Upton,

The Sarcoma Foundation of America (SFA) is pleased to submit these comments to the 21<sup>st</sup> Century Cures Initiative. We would like to thank you, as well as Rep. Diana DeGette and the Energy and Commerce Committee, for the willingness to undertake the process of looking at the state of biomedical innovation in the United States.

The Sarcoma Foundation of America, a 501(c)(3) nonprofit charitable organization, advocates for increased research to find new and better therapies with which to treat patients with sarcoma. The organization raises money to privately fund grants for researchers and conducts education and advocacy efforts on behalf of sarcoma patients. The SFA also interacts with public, private for-profit, and private non-profit entities to educate and raise awareness about the treatment needs of not only sarcoma patients, but also all patients with rare cancers and rare, life-threatening diseases.

Sarcoma is a rare cancer of the connective tissue (bone, muscle, nerve, blood vessel, tendon, fat) with about 14,000 new cases and 6,000 deaths each year. At any one time, 50,000 patients and their families are struggling with sarcoma. The disease is particularly rare in adults, comprising just 1 percent of all adult cancers. However, sarcoma is rather prevalent in children, making up approximately 15 percent of all childhood cancers. Adding to the difficulties in fostering new drug development, there are 50 validated histologic subtypes of sarcoma, with the potential for the existence of over 100 subtypes. This means that an already rare disease is further broken down into increasingly smaller subsets of patients. Unfortunately, sarcoma

is commonly hidden deep in the body, so it is often diagnosed when it has already become too large to expect a hope of being cured.

There is tremendous unmet medical need for sarcoma. It is sometimes curable by surgery or by surgery with chemotherapy and/or radiation, but about half the time is totally resistant to all of these approaches—thus the extreme need for new therapeutic approaches. Unfortunately, only one drug has been approved for the treatment of this cancer in the past 30 years in the United States. This approval came in 2012 when the Food and Drug Administration (FDA) gave full approval to Votrient for the treatment of soft tissue sarcoma. While this was a remarkable step forward for the treatment of adults with sarcoma, there is still no approved therapy for children with this rare cancer.

A significant contributing factor to the long gap in the approval for new therapies for sarcoma was, in part, due to the past reliance on overall survival (OS) as the primary endpoint for demonstrating clinical benefit for sarcoma. Given the small patient population, reaching OS was a challenge thanks to the difficulties in recruiting and retaining sufficient patient numbers to produce meaningful clinical trial data. Progression-free-survival (PFS) is a more realistic and attainable measure than overall survival for demonstrating clinical benefit for rare cancers like sarcoma. The SFA is encouraged that the FDA gave Votrient full approval using PFS as the endpoint. Combined with the language in FDASIA directing the FDA to improve access to the accelerated approval pathway, we are heartened that this signals a shift in approvals for drugs for sarcoma and will cement PFS as the regulatory approval standard. The SFA is hopeful that an increased focus on flexibility will remove uncertainty and encourage pharmaceutical companies to move forward on drug development for diseases like sarcoma.

A lack of investment in basic and translational research has also been a barrier to drug development for sarcoma. Overall, when accounting for inflation, the budget for the National Institutes of Health (NIH) has dropped 22 percent since 2003, and the National Cancer Institute's (NCI) budget has been cut by 24.7 percent. In 2012, the NCI's funding for sarcoma research fell to \$38.9 million from \$41.0 million in 2011. Unfortunately, less than 1 percent of the overall NCI budget in 2012 was dedicated to sarcoma research. While we know that funding for the NIH is not under the jurisdiction of this committee, we point out this issue as an obstacle to advancements for serious medical conditions like sarcoma.

Given these roadblocks, advocacy organizations like the SFA have had to take a very proactive role to see increased research and progress toward new and better therapies. Without an investment in research leading to drug development, patient groups are left to try and fulfill this unmet need. Since 2003, the SFA has invested more than \$5 million in research. Grants funded by the SFA have contributed to understanding and progress in every category of the process. Without a financial investment from the SFA, important basic science efforts – research not likely to be funded by the government or the pharmaceutical industry – may have gone unfunded. Also in an effort to better understand sarcoma, the SFA created the Sarcoma Patient Registry and has gathered detailed clinical information from patients who have this rare cancer. Patient information includes diagnosis, subtype,

and treatments. The goal is to use the Sarcoma Patient Registry to identify patients for clinical trials, and to use the data as a control arm of a clinical trial, to run an observational study, and to serve as a natural history study of the disease.

Because SFA has made it a priority to expedite the discovery of new treatments with which to treat sarcoma, we are taking the lead in creating an innovative research program in sarcoma sub-type genomic profiling and personalized therapeutics. This collaborative effort, known as Vision 2020, will join together academic, for-profit and non-profit partners. The genomic data derived from this effort will be used to identify specific genetic drivers of sarcomas, allowing patients to receive treatment where therapeutics exist for those genetic drivers, and identify new molecular targets for the development of novel, life-saving therapeutics. The SFA is in alignment with many other cancer experts in envisioning that proper cancer care needs to quickly evolve into individualized approaches and treatments relevant to each individual's disease. We welcome any legislative initiative that fosters reform in the Executive Branch health care regulatory bureaucracy consistent with this vision.

The SFA urges Congress to make the development and delivery of new life-saving therapeutics for patients with sarcoma and other rare diseases a national priority. There is significant need for increased funding for basic and translational research, as well as for an effort to provide the pharmaceutical industry with the best incentives to pursue new life-saving therapeutics in rare diseases. Patients with sarcoma and other rare diseases also need Congress to continue working with the FDA to improve the regulatory environment under which these new life-saving therapeutics are approved so that patients can have access to treatments as soon as possible. For patients like these, every day counts.

Once again, we thank you for the opportunity to submit these comments and share with you the challenges that have impeded the development of new and improved treatments for sarcoma patients. We also thank you for your interest in improving the state of biomedical innovation and take great interest in being a part of this process with you.

If you have any questions about these comments or about the work of the Sarcoma Foundation of America, please contact Lori Hoffman, Manager of Scientific and Government Affairs, at [REDACTED]

Respectfully submitted,

[REDACTED]

Bert Thomas, IV  
Chief Executive Officer