DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

Hearing on "21st Century Cures Implementation: Updates from FDA and NIH"

Witness appearing before the
House Committee on Energy and Commerce Subcommittee on Health

Francis S. Collins, M.D., Ph.D.
Director, National Institutes of Health

Accompanied by

Norman E. "Ned" Sharpless, M.D.
Director, National Cancer Institute

and

Stephanie Devaney, Ph.D.
Deputy Director, *All of Us* Research Program

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Chairman Burgess, Ranking Member Green, Distinguished Members of this Subcommittee, thank you for hosting this important hearing.

The 21st Century Cures Act (Cures Act) touches on so many important issues. From providing support for four cutting edge research priorities, to enhancing privacy protections to inclusion of various communities in research trials, to reducing administrative burden to expanded prize authority, we at NIH appreciate your leadership and dedication in enacting new authorities to speed the pace of research and improve how science is conducted to transform the way we translate discovery into therapies.

In my testimony, I will update you on how NIH is implementing some of the key provisions of the Cures Act and how it is benefiting the biomedical research community and, most importantly, patients and the general public.

Big Data: The Promise of Data Sharing Balanced With the Need for Privacy

As in most fields, computing power is changing the way research is done. The promise of big data cannot be overstated for finding patterns of disease and health and targeting therapeutics to sub-populations. The Congress, in the Cures Act, wisely recognized both the potential and the risks inherent in sharing data sets and NIH has moved quickly to get the appropriate protections in place.

First, on September 7, 2017 NIH issued a Guide Notice to our research community implementing the significant enhancements this Committee made to the Certificates of Confidentiality, making them both automatic and compulsory. To implement this change while minimizing the burden to our researchers, we streamlined the issuance of Certificates into the

terms and conditions of every research award we make involving human subjects.[1] Since October 1, 2017 every NIH award has this added layer of protection for research participants.

Second, on September 17, 2017 guidance on the FOIA exemption for genomic information was disseminated to all NIH FOIA officers.

Only now that the new Cures Act privacy protections are in place, are we moving forward on the exciting new authority to require data sharing. This will be a sea change in biomedical research so we must be deliberate about how to measure the usefulness of data sets, where shared data should be stored, how patient protections are insured, how interoperability is achieved, and what tools researchers most need in the shared environment. On November 6, 2017 NIH made 12 awards in a Data Commons Pilot to answer just these kind of questions. We selected three prominent NIH datasets researchers can use to test their processes. The biomedical research community will be watching this pilot program very closely.

Relatedly, this spring NIH published the Strategic Plan for Data Science,[2] a multi-year plan to make big data sustainable, interoperable, accessible, and usable. A key component of the Strategic Plan for Data Science is NIH's effort to hire a Chief Data Strategist. The Chief Data Strategist will report directly to the NIH Director and will lead the coordination of data science activities across NIH. We have seen exponential growth in biological sciences data production and look forward to meeting the challenges and leveraging the opportunities provided by data science in the months and years ahead. Through implementation of the Strategic Plan for Data Science, NIH will maximize the potential of existing data, enable new directions for research, increase accuracy, and support precision methods for healthcare.

[1] https://humansubjects.nih.gov/coc/index.
[2] https://datascience.nih.gov/sites/default/files/NIH_Strategic_Plan_for_Data_Science_Final_508.pdf.

Inclusion

We've made tremendous progress in managing diseases through the development of new drugs and devices over the years that were tested in clinical trials. But trials haven't always included the full spectrum of humanity, and this limits the applicability of study results. It also limits our ability to target therapies and address disparities. Congress helped NIH address this issue through the Cures Act in three focus areas: inclusion of children and seniors; inclusion of pregnant and lactating women; and continuing our focus on women, and racial and ethnic minorities.

On June 1-2, 2017 as required by the Cures Act, NIH held a workshop on inclusion across the lifespan. It might seem easy to include all age ranges but both children and older adults require special considerations. At the workshop, investigators with expertise in conducting clinical studies with pediatric and older populations, ethics experts, and other stakeholders had a robust discussion about barriers and facilitators to the inclusion of volunteers of all ages in research. The findings and recommendations were presented at my Advisory Committee meeting on December 14-15, 2017, and on December 19, 2017 we announced that we were revising the NIH Policy and Guidelines on the Inclusion of Children to apply to individuals across the lifespan.[3] The revisions broaden the policy to address inclusion of research participants of all ages and will apply beginning in January 2019 to all NIH-supported research involving human subjects.

The Cures Act also asks NIH to continue making progress on the inclusion of women and ethnic and racial minority populations in research. This has been a partnership of the Congress and NIH for many years – the Congress authorized both the NIH Office of Research on

[3] https://grants.nih.gov/grants/guide/notice-files/NOT-OD-18-116.html.

Women's Health and what is now the National Institute on Minority Health and Health Disparities in 1993. With the help of the Congress and the Cures Act, we continue to improve our monitoring and implementation of inclusion in these important areas. We are now collecting inclusion data on a study-by-study basis. In the coming year NIH will report, for the first time, inclusion data from studies on a disease and condition basis.

Finally, the Cures Act created a Task Force on Research Specific to Pregnant Women and Lactating Women (PRGLAC) to advise the Secretary of Health and Human Services regarding gaps in knowledge and research on safe and effective therapies for pregnant women and lactating women.[4] This area of research is vital, but it is absolutely critical that we carefully consider the risks of exposures in this potentially vulnerable time of life. NIH established PRGLAC on March 13, 2017 bringing together federal and non-federal experts, including the Food and Drug Administration, representatives from relevant medical societies, non-profit organizations, and industry, to discuss these important issues.

PRGLAC has already held four public meetings – the first on August 21-22, 2017 to determine the scope of current Federal research and regulatory activities on safe and effective therapies for pregnant and lactating women, the second on November 6-7, 2017 to understand the ethical issues surrounding research to develop therapies for pregnant and lactating women, the third on February 26-27, 2018 to discuss communication strategies for health care providers and the public about the use of therapies for pregnant and lactating women, and the fourth on May 14-15, 2018 to discuss recommendations to address the gaps in knowledge, ethical issues, and communication strategies for therapies used by pregnant and lactating women. In addition, NIH issued a Request for Information to further inform the task force's deliberations.

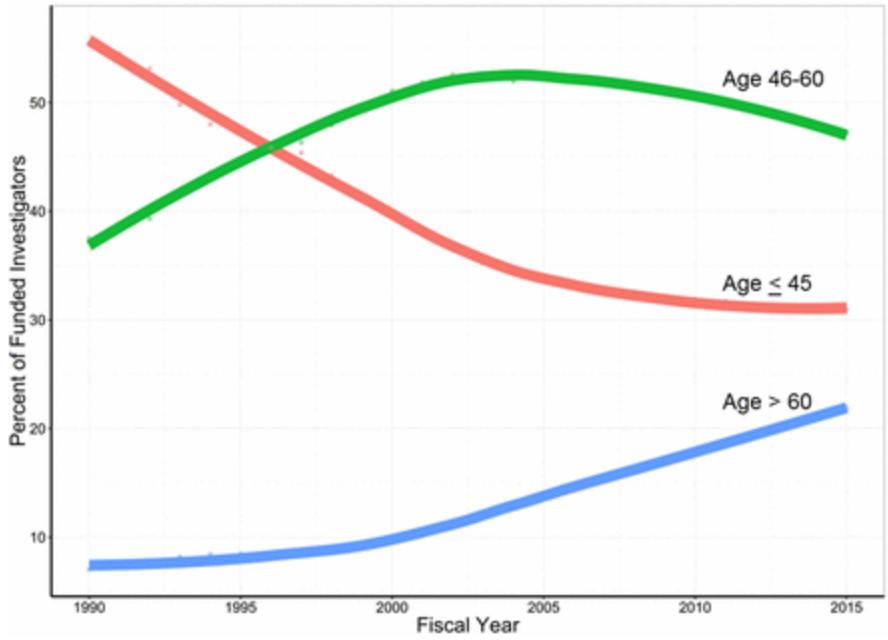
[4] https://www.nichd.nih.gov/about/advisory/PRGLAC/Pages/index.aspx.

Based on the outcome of the Task Force meetings, a report with the final recommendations has been developed and will be sent to the HHS Secretary and Congress by September 2018. NIH is grateful to the Congress for recognizing the need for careful consideration in this area of research and looks forward to addressing any recommendations made by the Task Force, as determined by the Secretary.

Strengthening Biomedical Workforce

NIH and its stakeholder community have for many years been concerned about the long-term stability of the biomedical research enterprise. As a consequence of NIH's loss of more than 20 percent of its purchasing power from 2003 to 2015, researchers were forced to vie for limited resources, leading to a hypercompetitive environment. With success rates below 20 percent, many highly meritorious applications were going unfunded. This too often resulted in misaligned incentives and unintended consequences for talented researchers at all career stages who were trying to succeed and stay in science. This kind of environment can be particularly challenging for many new- and mid-career investigators.

Over the last several years, NIH has taken numerous steps to balance, strengthen, and stabilize the biomedical research workforce, but these measures have only taken us so far. While by 2015 the percentage of NIH awards that support early-career investigators went from declining to flat, those gains were offset by a decline in the percentage of NIH awards that supported mid-career investigators.



As a direct result of the Cures Act, in June 2017 NIH launched the Next Generation Researchers Initiative[5] aimed at strengthening the biomedical workforce with a focus on early career investigators or investigators who are at an early stage in their career. NIH intends to take a multi-pronged approach, which we outlined in an article published on November 7, 2017,[6] to increase the number of NIH-funded early-stage investigators and to stabilize the career trajectory of scientists at all stages.

NIH is developing evidence-based, data-driven strategies to assure that NIH investments are directed in ways that maximize scientific output. We are being aided in these efforts by an expert Working Group of the Advisory Committee to the Director, who will present recommendations in December 2018. But several important steps are already being taken: Institutes and Centers are placing greater emphasis on current NIH funding programs to identify, grow, and retain new- and early-career investigators across these critical career stages. The NIH

[5] https://grants.nih.gov/ngri.htm.
[6] Michael Lauer, Lawrence Tabak, and Francis Collins, "Opinion: The Next Generation Researchers Initiative at NIH," *PNAS*, 114 (2017): 11801-11803.

Office of the Director is tracking progress across ICs in order to assess if these strategies are working. I am personally committed to this issue and thank the Committee for their support of early-career investigators.

System Innovation: Reducing Administrative Burden and Increasing Efficiency

The Cures Act provided NIH with new authorities to improve efficiencies and speed up the discovery process.

The Cures Act included provisions to improve ClinicalTrials.gov. ClinicalTrials.gov is a widely utilized database of privately and publicly funded clinical studies conducted around the world that plays a crucial role in helping to ensure the transparency and accountability to the public of researchers and their sponsors. In addition, this resource is used by researchers to stay up-to-date on developments in their field, find collaborators, and identify unmet needs. It is also used by patients and families to search for potential studies to enroll in or learn about new treatments that are being tested. NIH strives to make this resource as user friendly as possible so it can benefit researchers, patients, and their families, and the Cures Act is helping in several ways.

First, the Cures Act made technical fixes to the legislation establishing ClinicalTrials.gov that ensure NIH is able to capture more clinical trials in the system and improve our oversight and transparency. Second, it required NIH to consult with relevant Federal agencies and other stakeholders to receive recommendations to enhance ClinicalTrials.gov's usability, functionality, and search capability. In February 2017 the National Library of Medicine (NLM), along with 18F, a digital services consultancy within the General Services Administration, began conducting user research on ClinicalTrials.gov with a range of stakeholders. As a result of this

work, NIH rolled out a first in a series of changes to ClinicalTrials.gov on June 19, 2017. On September 25, 2017 and December 18, 2017 NLM released updates as the next phase in its ongoing effort to enhance the functionality of the database. In 2018 NLM added features for finding studies listed containing full protocols and other study documents and enhanced the information displayed about expanded access programs. In response to the Cures Act, NLM will work continuously to make it easier for users to find and participate in clinical trials.

In an effort to improve efficiency, the Cures Act provided a new EUREKA prize authority and allowed NIH to use Other Transactions Authority (OTA) in two areas that need extra flexibility and collaboration: the Common Fund and the *All of Us* Research program, part of the NIH Precision Medicine Initiative.

NIH, through the National Institute on Aging (NIA) began implementing the EUREKA prize authority in November 2017 through a request[7] for public input on (1) the feasibility of three potential prize competitions focused on Alzheimer's disease (AD) and related dementias (ADRD): Validating predictors of AD progression; PET radiotracer to measure in vivo synaptic integrity; and low cost innovation of improving systems of care for AD/ADRD patients and caregivers; and (2) any other suggestions on AD/ADRD research goals to connect to a prize. Comments were due on December 31, 2017. The NIA considered the comments gathered and decided to move forward with a prize competition focused on innovations that have the potential to improve care for people living with AD/ADRD through the creation of a widely accessible and innovative technology tool(s) that addresses unmet needs in care coordination and/or care navigation through the health system. On June 11, 2018 the NIA launched a public comment platform[8] to engage a broad audience in further discussion to optimize planning efforts for their

[7] https://grants.nih.gov/grants/guide/notice-files/NOT-AG-17-018.html.
[8] https://nia-research.ideascale.com/a/ideas/recent/campaign-filter/byids/campaigns/23294/stage/unspecified.

EUREKA prize competition. The purpose of soliciting additional public comments was to seek feedback on NIA's prize topic specifically as it related to (1) the possibility that this prize activity duplicates other ongoing activities in any relevant sector (e.g., academia, business), (2) the attractiveness of this question to a broad audience of possible solvers, (3) the length of time solvers would need to develop a prize submission, and (4) metrics that judges might use to identify a winner. Comments were due on July 1, 2018. The NIA is incorporating relevant input received into a final prize announcement for Challenge.gov, planned for release prior to September 31, 2018.

NIH also formed the EUREKA Prize Coordination Committee to review future proposals for future EUREKA prize competitions and funded the National Academy of Sciences (NAS) to study Innovation Prizes and Federal R&D with specific emphasis on strategies to determine which "EUREKA" prize topics are consistent with congressional intent. The NAS study will also consider the strengths and weaknesses of various measures of health outcomes and effects on government expenditures. The NAS intends to hold a workshop in 2018.

OTA is integral to our exploration of how best to structure data sharing, known as the Data Commons Pilot Phase,[9] which was announced on November 6, 2017. The goal of the NIH Data Commons is to accelerate new biomedical discoveries by providing a cloud-based platform where investigators can store, share, access, and compute on digital objects (data, software, etc.) generated from biomedical research and perform novel scientific research including hypothesis generation, discovery, and validation. The use of OTA awards has allowed flexibility for the awardees to work together to design innovation solutions that meet the computational and scientific needs of the Pilot.

[9] https://commonfund.nih.gov/bd2k/commons/awardees

The *All of Us* Research Program (described below) aims to enroll one million individuals in a decades-long research project. That ambitious goal requires flexibility, complex and dynamic interactions, and ways to engage non-traditional NIH awardees to advance the mission. For example, *All of Us* has used OTA to make awards to the Healthcare Provider Organizations to help build the research protocols, test enrollment procedures, and collect essential health data and biological specimens.

The Cures Act also recognizes that two of the cornerstones of scientific advancement are rigor in designing and performing scientific research and the ability to reproduce biomedical research findings. In recent years, the scientific community has become aware of the need to improve rigor and reproducibility. In 2014, NIH worked with scientific publishers to develop a set of principles and goals that 79 publishers have now endorsed. As the Cures Act requires, my Advisory Committee has convened a Working Group on Rigor and Reproducibility and they are reviewing the experience of the last few years, leading to the development of recommendations for a formal policy. I look forward to updating you as this effort takes shape.

NIH Innovation Fund

Last, but certainly not least, the Cures Act provided multi-year funding through the NIH Innovation Fund for four highly innovative scientific research initiatives: the Precision Medicine Initiative (PMI), the Brain Research through Advancing Innovative Neurotechnologies® (BRAIN) Initiative, the Cancer Moonshot, and the Regenerative Medicine Innovation Project. As required by the Cures Act, on March 28, 2017 I solicited recommendations from my Advisory Committee on how to allocate the funds. We had a robust conversation about each of the initiatives and the Advisory Committee members provided critical advice on how to move

forward. As a result of that discussion, and conversations with my NIH colleagues, we drafted the NIH Innovation Fund Work Plan,[10] which was submitted to Congress in September 2017 outlining how the agency will use the NIH Innovation Funds for each of these four initiatives. I would like to tell you a bit about each of these initiatives and how the NIH Innovation Funds are helping to move each initiative forward.

The Precision Medicine Initiative

Precision medicine is a revolutionary approach for disease prevention and treatment that takes into account individual differences in lifestyle, environment, and biology. While some applications of precision medicine have found their way into practice over the years, this individualized approach is simply not available for most diseases. The *All of Us* Research Program, a key element of PMI, is building a national resource—one of the world's largest, most diverse biomedical data sets in history—to accelerate health research and medical breakthroughs, enabling individualized prevention, treatment, and care. *All of Us* will enroll one million or more U.S. volunteers from all life stages, health statuses, races/ethnicities, and geographic regions to reflect the country's diverse places and people to contribute their health data over many years to improve health outcomes, fuel the development of new treatments for disease, and catalyze a new era of evidence-based and more precise preventive care and medical treatment.

Across the nation, NIH has engaged 10 large health provider organizations, six community health centers, and the Veterans Health Administration to be our partners in this ambitious study. The program has funded over 30 community partner organizations to motivate

[10] https://www.nih.gov/sites/default/files/research-training/initiatives/nih-cures-innovation-plan.pdf.

diverse communities to join and remain in the program, with a focus on those traditionally underrepresented in biomedical research.

We began a robust, year-long beta phase in May 2017, during which each of our partners were able to test their systems and processes to ensure a good experience for participants. I am excited to tell you that *All of Us* launched nationally on May 6, 2018 with events across the country to mark the program's open enrollment. As of July 16, 2018, 85,369 individuals have started the enrollment process, and 42,315 have completed all the steps in the protocol. Of those, I'm thrilled to tell you that 70-75% are from communities who have been historically underrepresented in biomedical research and almost 50% are specifically from racial/ethnic groups who have not been included in research.

Following the national launch, we continue to improve and adjust the program based on participant feedback and emerging scientific opportunities and technological advances. We also are currently building the All of Us data resource, which is designed to be used by a broad range of researchers to study complex risk factors, support ancillary studies and clinical trials, and link to other large data sets. The Cures Act Innovation Funds will be critical to ensuring the success of *All of Us* and the promise of personalized medicine.

The BRAIN® Initiative

The BRAIN Initiative is revolutionizing our understanding of the human brain, the most complex structure in the known universe. Launched in 2013, this large-scale effort is pushing the boundaries of neuroscience research and equipping scientists with insights necessary for treating a wide variety of brain disorders. By accelerating the development and application of innovative technologies, researchers are producing a revolutionary new dynamic picture of the

brain that, for the first time, shows how individual cells and complex neural circuits interact in both time and space. Long desired by researchers seeking new ways to treat, cure, and even prevent brain disorders, this picture is filling major gaps in our current knowledge and providing unprecedented opportunities for exploring exactly how the brain enables the human body to record, process, utilize, store, and retrieve vast quantities of information, all at the speed of thought.

NIH leveraged the Cures Act's FY 2017 Innovation Funds, in addition to our annual appropriation, to launch 110 exciting new research projects[11] and in FY 2018 NIH expects to fund approximately 150 new BRAIN Initiative projects. Cures funds will support critical areas including data infrastructure and sharing, the BRAIN Initiative Cell Census Network (which is developing an atlas of brain cell types), the Team Research Brain Circuits Program, and human brain studies. In human studies, the BRAIN Initiative is advancing brain imaging and non-invasive brain stimulation, and public private partnerships are investigating self-adjusting implanted brain stimulation therapies that are already showing promise. Ultimately, this will lead to an increased understanding of brain health, and a means of preventing brain disorders such as Alzheimer's disease, Parkinson's, schizophrenia, autism, drug addiction, and traumatic brain injury.

The Cancer Moonshot℠

The Cancer Moonshot,[12] funded in the Cures Act, has an ambitious goal: to dramatically speed advances in cancer prevention, diagnosis, treatment, and care. To identify the most promising and innovative strategies, the National Cancer Institute (NCI) solicited direct input from the

[11] https://www.braininitiative.nih.gov/funding/fundedAwards.htm.
[12] https://www.cancer.gov/research/key-initiatives/moonshot-cancer-initiative.

public and convened a Blue Ribbon Panel (BRP) of the nation's top cancer researchers, oncologists, patient advocates, and private-sector leaders. In September 2016, the BRP presented its report outlining ten ambitious and achievable recommendations to the NCI's National Cancer Advisory Board. These recommendations have shaped the scientific blueprint of the Cancer Moonshot representing areas of research that are poised to accelerate our understanding of cancer and bring benefit to patients. Overall, the recommendations create a vision for future cancer research and treatment in which:

- Researchers can identify possible targets for the development of new cancer treatments and preventive interventions, including immunotherapy and immunoprevention, and learn more about how to avoid or overcome cancer drug resistance in patients;
- Diverse groups of patients contribute information about their cancer, obtain a genomic profile, learn what treatments might work best given their profile, and identify clinical trials that may be appropriate for them;
- Infrastructures are established so that health care providers and researchers can share, access, and analyze information that improves the understanding of how tumors evolve, better predicts treatment outcomes, and helps control patient symptoms and side effects.

Some of these goals are scientific in nature, and some are systemic. If we are to speed advances, we cannot simply do more of the same. We must transform the way we conduct research, the way we share results, and the way we get discoveries into patient care. In FY 2017 NIH made 142 Cancer Moonshot awards, and in FY 2018 NIH issued 17 Cancer Moonshot Funding Opportunity Announcements, including exciting opportunities in immuno-oncology for both adult and pediatric populations, and specific efforts to tackle drivers of childhood cancer.

In FY18, Innovation funds will be used to support the development of both adult and pediatric immunotherapy networks to accelerate the discovery of new immune targets and evaluate novel immune-based therapies for adults, and to identify and advance research opportunities for translating immunotherapy concepts for children and adolescents with cancer. In addition to these collaborative team science efforts, NCI is also supporting the development of a consortium to advance our understanding of the biology and mechanisms of action of fusion oncoproteins in pediatric cancers, and to apply this knowledge toward developing targeted therapeutic approaches. Increased attention to this important but understudied field can help overcome existing barriers to progress and pave the way for novel therapeutic approaches with increased efficacy and fewer side effects than current options.

With the support of the Congress, the Cancer Moonshot will transform the way cancer research is conducted and ensure that substantial progress is made for patients and their families.

The Regenerative Medicine Innovation Project

Regenerative medicine is an emerging area of science that holds great promise for treating and possibly even curing a variety of injuries and diseases. Regenerative medicine includes using stem cells and other technologies, such as engineered biomaterials and gene editing — to repair or replace damaged cells, tissues, or organs. Stem cell-based approaches are under development in labs around the world, and some have already moved into clinical trials. Such progress notwithstanding, much work remains to be done toward the development of safe and effective regenerative medicine interventions to realize the full potential of this field.

As a result of the Cures Act, NIH launched the Regenerative Medicine Innovation Project (RMIP) to support clinical research using adult stem cells while promoting the highest standards

for carrying out scientific research and protecting patient safety. The $2 million Cures provided for this initiative in FY 2017 were amplified through matching funds and NIH Institute contributions to support research totaling $5.4 million. NIH has worked in close collaboration with the FDA to implement the RMIP. In September, NIH made eight clinical research awards[13] that cover a broad spectrum of science and new technologies, and have the potential to advance understanding and treatment of common diseases – including diabetes, anemia, corneal and other eye diseases, and chronic skin ulcers – as well as rare diseases, including idiopathic pulmonary fibrosis, inherited skin diseases, and sickle cell disease.

Several awards will explore the use of adult stem cells to make specialized cells and tissues that could help reduce the need for whole organ transplants or otherwise restore normal function. Others aim to develop reliable methods of generating platelets and optimizing red blood cell production in the lab to improve the safety and supply of blood available for transfusion.

To inform future funding decisions, NIH and FDA hosted a workshop in December 2017[14] to explore the state of regenerative medicine science involving adult stem cells, with a focus on promising approaches for the development of safe and effective products, scientific areas poised for major transformative advances, and critical gaps that must be addressed to enable significant innovation and rapid advancement of the field. A Funding Opportunity Announcement for new awards will be issued in FY 2018 and we anticipate the remaining authorized RMIP funds ($28 million) will support up to 15 projects, including both late-stage pre-clinical studies and early-phase clinical trials.

[13] https://www.nih.gov/rmi/fy-2017-funded-awards.
[14] https://www.nih.gov/research-training/medical-research-initiatives/cures.

In addition, we are establishing a collaborative network of entities, an "RM Innovation Catalyst," to provide much needed clinical services to support RMIP awardees, including in-depth stem cell characterization, support to address regulatory requirements, manufacturing assistance for preparation of clinical grade stem cell products, and storage and sharing of clinical data. NIH looks forward to the opportunity the Cures Act provides to significantly advance this field of science.

Conclusion

Thank you for your leadership and dedication that resulted in enacting the Cures Act 18 months ago. The Cures Act has provided NIH with critical resources and tools to advance our mission – to seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability. We appreciate Congress's support for NIH through the Cures Act and will continue to implement the law to accelerate scientific discoveries and develop new approaches to the prevention, treatment, and cure of disease.