Implementation of Funding Plan for the NIH Innovation Projects Under the 21st Century Cures Act

As part of developing the accountability and oversight work plan for the NIH Innovation Projects authorized by Section 1001 of the 21st Century Cures Act, the NIH Director was required to solicit recommendations from the Advisory Committee to the (NIH) Director (ACD) on the allocation of funds, the contents of the work plans, and whether the proposed projects link appropriately to the NIH-Wide Strategic Plan (see appendix I for relevant Cures Act language).

Support for four innovation projects was authorized by the Act:

1. *Precision Medicine Initiative*[1] *(PMI)* – is a historic effort to gather data from one million or more people living in the United States to accelerate research and improve health. By taking into account individual differences in lifestyle, environment, and biology, researchers will uncover paths toward delivering precision medicine.

2. The *Brain Research through Advancing Innovative Neurotechnologies*® *(BRAIN) Initiative* – is aimed at revolutionizing our understanding of the human brain. By accelerating the development and application of innovative technologies, researchers will be able to produce 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 will fill major gaps in our current knowledge and provide 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.

3. The *Beau Biden Cancer Moonshot℠* – will accelerate cancer research to make more therapies available to more patients, and to improve our ability to prevent cancer and detect it at an early stage.

4. *Regenerative Medicine* – NIH, in coordination with the FDA, will award grants and contracts for clinical research to further the field of regenerative medicine using adult stem cells, including autologous stem cells.

[1] Precision Medicine Initiative and All of Us, are service marks of the U.S. Department of Health and Human Services.

The total funding is $4.8B over a 10-year period. Funds are placed in an NIH Innovation Account, and must be appropriated each year. The funds do not count against the budget caps. Funding for the projects is summarized in the following table:

Funding for NIH Innovation Projects under the Cures Act				
Fiscal Year	**Precision Medicine Initiative**	**BRAIN**	**Cancer Moonshot**	**Regenerative Medicine**
2017	$40,000,000	$10,000,000	$300,000,000	$2,000,000
2018	$100,000,000	$86,000,000	$300,000,000	$10,000,000
2019	$186,000,000	$115,000,000	$400,000,000	$10,000,000
2020	$149,000,000	$140,000,000	$195,000,000	$8,000,000
2021	$109,000,000	$100,000,000	$195,000,000	
2022	$150,000,000	$152,000,000	$194,000,000	
2023	$419,000,000	$450,000,000	$216,000,000	
2024	$235,000,000	$172,000,000		
2025	$36,000,000	$91,000,000		
2026	$31,000,000	$195,000,000		
TOTAL	**$1,455,000,000**	**$1,511,000,000**	**$1,800,000,000**	**$30,000,000**

On March 28, 2017, the ACD met to review the work plans for the NIH Innovation Projects. Each work plan was presented to the ACD by the Director of the NIH Institute or Office that is responsible for the innovation project. Following the presentation, ACD members were given the opportunity to ask questions or provide comments on the work plans. Most ACD questions focused on gaining clarity on specific aspects of the Innovation Projects (for example, the types of biospecimens that will be collected in the *All of Us* Research Program). ACD members also made minor recommendations to some work plans. Following discussion, the ACD unanimously voted to approve all the Innovation Project work plans. The ACD recommendations have been incorporated into the work plans described in this document, which will be submitted by the NIH Director to the Congress within 180 days after enactment of the Act (see Appendix I for excerpt of specific language). That deadline will be reached on June 11, 2017.

I. Precision Medicine Initiative: *All of Us* Research Program

A. Overview

Far too many diseases do not have a proven means of prevention or effective treatment. We must gain better insights into the biological, environmental, and behavioral influences on these diseases to make a difference for the millions of people who suffer from them. Precision medicine is a revolutionary approach for disease prevention and treatment that takes into account individual differences in lifestyle, environment, and biology. While some advances in precision medicine have been made, the practice is not in use for most diseases.

The *All of Us* Research Program is a key element of the Precision Medicine Initiative (PMI). Based on the recommendations from the Advisory Committee to the Director Precision Medicine Initiative Working Group report[2], the *All of Us* Research Program 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 engage 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.

Gathering in-depth, constantly-evolving data from volunteers over many decades—from electronic health records, biospecimens, and questionnaires, to physical measurements, sensors, imaging, and wearable technologies—the program is expected to catalyze thousands of studies over time at the intersection of lifestyle, environment, and biological factors including genetics. This unprecedented scientific resource will produce fundamental knowledge that will help us better understand health and disease, and ultimately lead to individualized prevention, treatment, and care across the major common, and many of the rare, conditions we face today.

B. Innovation Account Funds

The 21st Century Cures Act authorizes the appropriation of $1.455 billion over 10 years (FY 2017-FY 2026) "[f]or the Precision Medicine Initiative, including for the advancement of a cohort of individuals to support the goals of the Precision Medicine Initiative."

As originally planned and conceived, the *All of Us* Research Program ten-year budget was projected to ramp up to $430 million per year to deliver the most value to researchers and participants. Expanding the infrastructure and network of more than 100 health provider and community support organizations to include and retain people from across the country costs approximately $160M annually. The big data systems that provide access to secure, de-identified data and easy-to-use tools for researchers (e.g., citizen scientists, community colleges, academic medical centers) will cost approximately $60M per year.

Using the 21st Century Cures Act funding, NIH will support multiple aspects of the *All of Us* Research Program, including: enrollment and retention of participants, collection and storage of data and specimens, evaluation of the program, and generation of biological data including genotyping and whole genome sequencing pilots. The Innovation Project funds

[2] *The Precision Medicine Initiative Cohort Program – Building a Research Foundation for 21st Century Medicine* https://www.nih.gov/sites/default/files/research-training/initiatives/pmi/pmi-working-group-report-20150917-2.pdf

authorized under the Cures Act are "no-year" funds, providing flexibility for when the funds can be obligated. To ensure responsible use of our resources, NIH will utilize a variety of strategies in obligating funding to the Program, including the use of carry over funds from some fiscal years. We will also learn from the experiences of *All of Us*, including participant experience and feedback from researchers, and will iterate and adapt in response. Therefore, all figures should be considered estimates that may be revised based on new information.

Funding for Precision Medicine Innovation Project under the Cures Act			
Fiscal Year	**Innovation Project Funds**	**Estimated Obligations**	**Estimated Carryover**
2017	$40,000,000	$21,500,000	$18,500,000
2018	$100,000,000	$118,500,000	$0
2019	$186,000,000	$139,400,000	$46,600,000
2020	$149,000,000	$195,600,000	$0
2021	$109,000,000	$101,000,000	$8,000,000
2022	$150,000,000	$158,000,000	$0
2023	$419,000,000	$312,000,000	$107,000,000
2024	$235,000,000	$177,000,000	$165,000,000
2025	$36,000,000	$190,000,000	$11,000,000
2026	$31,000,000	$42,000,000	$0
TOTAL	**$1,455,000,000**	**$1,455,000,000**	

C. Research Categories

Specific categories of *All of Us* research activities to be undertaken with Innovation Project funds include:

***All of Us* Activity**	**Innovation Project Funds** (numbers are approximate)
Health Care Provider Organization Network	$479,000,000
Engagement Partners	$50,000,000
Outreach to Participants and Researchers	$25,000,000
Biobank	$422,000,000
Data and Research Center	$237,000,000
Best Practices Research and Publication	$29,000,000
Biological Factors including Genetic Analyses	$148,000,000
Consumer/Mobile Technologies	$65,000,000

i. **Health Care Provider Organization Network (~$479M) –** Health Care provider organizations (HPOs) are foundational to the *All of Us* Research Program. HPOs are responsible for scientific input, collaborating on engagement and enrollment, communication, biospecimen collection, healthcare data collection, and participant retention. The Cures funding will support five Regional Medical Center HPOs as well as eight small Regional Medical Centers, including four to six Federally Qualified Health Centers. Expanding the HPO

network is top priority for the program to ensure that the geographic distribution of enrollment centers is as diverse as possible across the United States and includes healthcare organizations that are not typical applicants for NIH funding. This network will be essential for attaining our goal of a million or more participants that reflect the diversity of the United States within five years.

ii. **Engagement Partners (~$50M) –** To ensure the largest value of *All of Us* to researchers and participants, we must have a diverse participant pool. Engagement partners will increase awareness, educate, and motivate volunteers to join and remain in the program, and facilitate enrollment where needed. These partners will also engage and educate health care professionals (physicians, nurses, physician assistants, etc.) about the *All of Us* Research Program, as well as enable health care professionals to facilitate enrollment of their patients in the program. Cures funding to support engagement partners that can focus on those who are traditionally underrepresented in biomedical research will allow *All of Us* to enroll the diverse cohort needed.

iii. **Outreach to Participants and Researchers (~$25M) –** *All of Us* will utilize Cures funding to raise awareness among the community of potential participants and their intermediaries among the public. These efforts will reinforce the importance of maintaining active involvement with the program after initial enrollment. In addition, the program will seek to raise awareness among the research community about the availability of the dataset and biospecimens to be used for analyses, opportunities for ancillary studies, integration of innovative technologies for new data capture, and for clinical trial recruitment.

iv. **Biobank (~$422M) –** Biospecimens will be an important asset for *All of Us* allowing the program to generate many data types, as well as allowing other researchers to propose assays with the stored specimens. The Biobank at the Mayo Clinic has state of the art methods, technologies, and robotics for sample processing, handling, management, and storage as well as providing all materials needed for biospecimen collection. Cures funding will support the continued functioning of the biobank including access of samples to researchers across the country.

v. **Data and Research Center (~$237M) –** The Data and Research Center at Vanderbilt University acquires, store, organizes, and provides secure access to datasets and provides research support for the scientific data and analysis tools of the *All of Us* Research Program. We will utilize Cures funding to enhance the Data and Research Center's support of diverse research communities including academic researchers across disciplines, citizen scientists, industry, patient advocacy groups, data scientists, and technologists. Each of these user groups will require specialized tools to enable efficient access to the program data gathered for participants for analysis or innovation research.

vi. **Best Practices Research and Publication (~$29M) –** Evaluation of the *All of Us* program is essential to continued success and enhancement of the program. A portion of the Cures funding will be utilized to ensure the program and its components are properly evaluated from the outset for ways to improve their functioning, and to develop plans for implementing changes to ensure that *All of Us* is providing optimal value to participants and researchers.

vii. **Biological Factors including Genetic Analyses (~$148M) –** Under this scenario, *All of Us* will begin generating genomic data on participants in FY 2018

and begin implementation of the full genomic strategy in FY 2020. Starting in FY 2023, *All of Us* will utilize Cures funding to generate whole genome sequence data on a subset of participants. Assuming the continued downward trajectory of the cost of genome-sequencing technologies *All of Us* can extend this to approximately 300,000 participants through FY 2026.

viii. **Consumer/Mobile Technologies (~$65M) –** Given the prevalence and increased biosensing capabilities on everyday smartphones and fitness wearables, consumer and mobile technologies are a rapidly expanding source of valuable data for both participants and researchers. *All of Us* will use Cures funding to pilot the collection and linkage of mHealth data to other participant data received through the program and help pioneer tools, methods, and comparative studies that inform all researchers how to integrate and leverage mHealth data for scientific studies.

The *All of Us* Research Program and the activities funded through the Cures Act will support the National Institutes of Health Strategic Plan Objective 1: Advance Opportunities in Biomedical Research by providing an unprecedented research resource, advancing NIH's biomedical research agenda to improve health and prevent disease.

II. Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative

A. Overview

Despite remarkable insights about how individual brain cells and synapses work, neuroscience has had less success decoding how neural circuits carry out complex, higher functions of the brain and what goes wrong in neuro/mental/substance abuse disorders. Human brains have over 85 billion cells making over 100 trillion connections, and a major barrier to progress has been the inability to adequately define the structure of brain circuits and record the complex information flowing through them. The BRAIN Initiative®, announced in April 2013, arose because tools to tackle these challenges are now emerging, building upon advances from diverse fields of science and technology. The Initiative coordinates investment across multiple NIH Institutes, Federal agencies, and private groups, and has spurred multiple international brain research efforts.

Specific goals for NIH contributions to the Initiative were formulated over a year-long planning process that culminated in the release of BRAIN 2025: A Scientific Vision, a foundational planning document produced by a working group of the Advisory Council to the NIH Director (ACD). The 12-year roadmap lays out seven high-level research priorities and a professional judgment budget together with detailed rationale, sub-goals, and milestones. NIH continues to be guided by this document and by input from the Advisory Councils of the ten NIH Institutes and Centers (ICs) that contribute to the Initiative and that are represented on the BRAIN Multi-Council Working Group (MCWG). NINDS and NIMH serve as co-leads of the group of BRAIN ICs implementing the Initiative and as co-chairs of the MCWG, and a fulltime Director of the NIH BRAIN Initiative is being sought. In reviewing this Work Plan, the ACD suggested that NIH revisit the BRAIN 2025 plan. NIH is beginning an assessment of the BRAIN Initiative and as part of this effort, will revisit the report's priorities given progress to date, emerging scientific opportunities, and the evolving neuroscience landscape.

B. Innovation Account Fund

The 21st Century Cures Act authorizes $1.511 billion over 10 years for the BRAIN Initiative. NIH is taking a flexible approach for the Innovation Project funds to be used in combination with regularly-appropriated funds for the BRAIN Initiative. In FY 2016, this regular appropriation amounted to $150M as part of the base budget of the BRAIN Initiative ICs. In FY 2017, the regular appropriation rose to $250M.

To advance the goals of the Initiative, *BRAIN 2025* recommended that support be ramped up over the first several years with a sustained high level of investment following this initial increase. NIH proposes a similar approach for the BRAIN Innovation funding, and will use a variety of strategies to ensure that all projects supported with Innovation Project funds are fully funded by FY 2026. For example, money may be used for competing funds, for non-competing funds to support funded projects' out-years, and to support some multi-year projects at their outset, particularly in years where there are ample funds (e.g., FY 2023) and/or as we approach FY 2026. In addition, NIH may offer one-year administrative and/or competitive supplements for activities such as developing infrastructure, disseminating technologies to take advantage of new opportunities, and/or to accelerate

progress toward meeting some of the goals of the Initiative.

Each scientific goal is critical to the integrated purpose of the BRAIN Initiative, but different goals require different types and amounts of resources and funding. Progress in different areas may also occur at different rates and during different stages of the Initiative. For example, initial instrumentation and technology costs are expected to be particularly high in developing new recording methods for use in humans and improving techniques to create circuit maps of whole brains. Over time, the Initiative will increasingly transition to concerted, team-science application of promising research methods with the need for more sophisticated data management, analysis, and data sharing approaches. Supporting development of infrastructure for data science and data sharing platforms will be large-scale, high-cost projects. Dissemination of new technologies may best be addressed by multiple strategies including training courses, supplements to NIH-funded grants, and/or establishment of centers to help investigators adopt and utilize new technologies. Moving new technologies into human testing, projected to accelerate after 2020, will also require addressing additional scientific and regulatory hurdles, with higher associated costs.

It is quite likely that one or more of these areas may be ripe for development or acceleration during a period of Innovation Project fund increase (e.g., FY 2023). NIH will continue to examine the changing needs and highest priorities of the Initiative each year, and will plan a major mid-course review to integrate additional expert suggestions to ensure the BRAIN Initiative keeps pace with the evolving neuroscience landscape. This input will enable NIH to consider if scientific opportunities warrant the use of Innovation Project funds to support or accelerate a specific area of research.

Funding for BRAIN Initiative Innovation Project under the Cures Act			
Fiscal Year	Innovation Project Funds	Base Appropriation	ACD WG Recommendation
2017	$10,000,000	$250,000,000	$300,000,000
2018	$86,000,000	TBD	$400,000,000
2019	$115,000,000	TBD	$400,000,000
2020	$140,000,000	TBD	$400,000,000
2021	$100,000,000	TBD	$500,000,000
2022	$152,000,000	TBD	$500,000,000
2023	$450,000,000	TBD	$500,000,000
2024	$172,000,000	TBD	$500,000,000
2025	$91,000,000	TBD	$500,000,000
2026	$195,000,000	TBD	--
TOTAL	**$1,511,000,000**	**TBD**	**$4,000,000,000**

C. Research Categories

In agreement with the *BRAIN 2025* budget estimate, NIH plans to target 10% of Innovation Project funds to research infrastructure, with the remainder divided equally between

neurotechnology development and the application of novel neurotechnologies to understand brain circuit function in health and disease. At a more granular level, the seven priority areas of the Initiative, with associated best estimate breakdown of Innovation Project fund expenditures over the period from FY 2017- FY 2026 is shown below:

BRAIN 2025 Priority Area	Innovation Project Funds
Discovering Diversity	$150,000,000
Maps at Multiple Scales	$150,000,000
The Brain in Action	$150,000,000
Demonstrating Causality	$100,000,000
Identifying Fundamental Principles	$75,000,000
Advancing Human Neuroscience	$386,000,000
From BRAIN Initiative to the Brain	$500,000,000

i. **Discovering Diversity ($150M)**: Identify and provide experimental access to the different brain cell types to determine their roles in health and disease.

Investments by the BRAIN Initiative to-date have resulted in an array of innovative, high-throughput approaches to identify various characteristics of a cell that allow it to be classified: its shape, cellular components, behavior, and connections with other brain cells. Over the next 1-4 years, the Innovation Project funds will enable launch of the BRAIN Initiative Cell Census Network, a consortium of investigators focused on: 1) creating a comprehensive 3D mouse reference brain cell atlas that integrates molecular, anatomical, and physiological information, and (2) laying the groundwork for human and non-human primate reference brain cell atlases. Over years 5-9, NIH will support efforts to complete the mouse brain atlas and produce a cell census for selected brain regions in non-human primates and humans. Researchers could use Innovation Project funds to build on this work, and push for a full cell census of the human brain, which is at least three orders of magnitude larger in size and cell number than that of the mouse.

ii. **Maps at Multiple Scales ($150M)**: Generate circuit diagrams that vary in resolution from synapses to the whole brain.

Information flows through brain circuits to be stored, retrieved, processed, and acted upon. Information processing occurs at spatial scales ranging from synapses, to local circuits, to networks that span the entire brain. Understanding these circuits – both anatomically and functionally – is a critical goal for the Initiative. Over the next 1-4 years, investments from the Innovation Project funds will allow researchers to create, enhance, and validate tools to visualize and manipulate individual cells or tightly defined cell circuits, with increasing focus on human and non-human primate brain circuits. In years 5-9, researchers could begin using these tools to identify when and how circuits are disrupted in disease, and possibly develop new biomarkers to identify and track disease progression.

Creation of comprehensive brain atlases, coupled with brain-wide circuit-level maps of human and non-human primate brains, would be a landmark achievement for NIH and for neuroscience.

iii. **The Brain in Action ($150M)**: Produce a dynamic picture of the functioning

brain by developing and applying improved methods for large-scale monitoring of neural activity.

Thousands to millions of neurons are thought to engage to enable our most complex behaviors. Over the next 1-4 years, investments from the Innovation Project Fund in technology development will greatly enhance the ability to record from larger numbers of neurons in behaving animals and in humans undergoing physiological monitoring for clinical indications, i.e. epilepsy monitoring, deep brain stimulation. In years 5-9, researchers could deploy Innovation funds to record from whole regions of human brain through new implantable devices or via novel, minimally invasive technologies.

iv. **Demonstrating Causality ($100M)** – Link brain activity to behavior with precise interventional tools that change neural circuit dynamics.

One of the most exciting advances in the BRAIN Initiative is the development of new tools to turn on or off specific neurons with precision to define their role in a given behavior. Over the next 1-4 years, Innovation Project funds could be used to continue refinement of these reversible, non-invasive technologies to modulate brain activity with a wide array of stimuli including ultrasound, pharmaceutical approaches, and/or magnetic waves. Longer term investments over years 5-9 include use of these technologies by teams of scientists to build a comprehensive working knowledge of brain circuits responsible for language, memory, movement, and emotion.

v. **Identifying Fundamental Principles ($75M)** – Produce conceptual foundations for understanding the biological basis of mental processes through development of new theoretical and data analysis tools.

The dynamic activity of massively interconnected ensembles of neurons in specially organized networks gives rise to the internal states we experience as sensations, perceptions, emotions, thoughts, memories, and movements. The ability to record from large numbers of neurons during defined behaviors, combined with the ability to modulate specific neurons to detect how they alter or produce behaviors, will uncover the "language of the brain." Dysfunction of information processing in these neural circuits is the basis of neural and mental disorders. Over the next 1-4 years, initial investments with Innovation funds could include computational analyses of brain circuit activity via small, two-year exploratory research grants and large, team-based grants. These studies could reveal, for the first time, the fundamental principles of information processing underlying complex brain functions. If they progress to meet their milestones, these larger projects could require additional investments for years 5-9 to deliver predictive models that explain the basis of our thoughts and actions.

vi. **Advancing Human Neuroscience ($386M)**: Develop innovative technologies to understand the human brain and treat its disorders; create and support integrated human brain research networks.

A primary goal of the BRAIN Initiative is the acquisition of basic knowledge about how the healthy brain works, so we might gain a better understanding of – and

potential to intervene in – brain dysfunction in disease. The Initiative's investment in patient research with invasive and non-invasive recording and stimulation methods and on brain imaging reflects many of the *BRAIN 2025* priority areas. The immediate goals are to understand better how existing non-invasive stimulation techniques affect brain circuitry in patients and to develop new methods to non-invasively modulate circuits. Initial investments through BRAIN yielded transformative ideas for next generation human brain imaging that are now in planning or proof of concept stages. Over the next 1-4 years, Innovation Project funds could be used to support the expansion and implementation of these exciting new technologies through interdisciplinary teams, with academic-industry partnerships encouraged. We will also fund translational projects with the potential to provide new or enhanced therapeutic benefit in a variety of disorders, including Parkinson's disease, essential tremor, epilepsy, obsessive-compulsive disorder, cognitive impairment stemming from traumatic brain injury, and stroke recovery. Exciting advances in brain-machine interfaces aim for fully implanted devices allowing more natural movement for people who are paralyzed, and to restore sight in visually-impaired individuals. Over the next 5-9 years, NIH will leverage Innovation Project funds to support additional trials along these lines in close collaboration with FDA and through public-private partnerships.

vii. From BRAIN Initiative to the Brain ($500M): Maximizing the value of the BRAIN Initiative by integrating new technological and conceptual approaches produced in Goals #1- 6 to discover how dynamic patterns of neural activity are transformed into cognition, emotion, perception, and action.

As described in the previous sections, the BRAIN Initiative is integrating technologies and conceptual approaches on all fronts, ranging from mapping cell types and monitoring circuits for understanding their function, to technology dissemination and therapy development. The investment from the Innovation Project funds across the research priorities and core principles endorsed by the NIH ACD will rapidly accelerate progress toward the Initiative's goals.

The ACD Working Group identified core principles that cut across the seven scientific priority areas and are important to support and enhance the goals of the Initiative. The principles listed below also require an investment of funds over time. NIH will carefully manage the Innovation Project Fund to ensure the highest return on the taxpayer investment and achievement of the goals endorsed by the ACD. As with the seven priority areas, in a given year, the balance of the investment of funds across the options outlined below will depend on the scientific opportunities and the quality of the applications submitted.

i. *Establish platforms for preserving and sharing data*
BRAIN Initiative projects are on course to increase significantly the yield of data and research tools for the neuroscience community. Over the next 1-4 years, NIH will invest in projects to enhance data sharing and analysis of large data sets of neural activity linked to behavior. Because molecular, physiological, anatomical, and other types of data present very different informatics challenges, the initial focus will be on developing common standards and archives for each type of data. We will also support efforts to develop new data analysis and visualization tools, including data integration strategies. Over the subsequent 5-9 years, NIH could use Innovation

Project funds to move more aggressively to enable widespread data sharing across the research communities involved in BRAIN, e.g. neuroscience, engineering, mathematics, chemistry, and more. For example, we could invest in the central IT platforms and infrastructure to link and coordinate the various databases that will be developed for the different types of data produced by the Initiative.

ii. *Educate, validate and disseminate technology*
A critical factor for the long-term legacy of the BRAIN Initiative is the dissemination of new experimental technologies. From the start, the Initiative has convened scientific meetings to encourage collaboration, and has funded graduate student and post-doctoral investigators on project teams who will carry new ideas and methods as they move on in their careers. Building strength in quantitative neuroscience, attracting new investigators from the quantitative disciplines, and educating investigators to apply sophisticated tools in rigorous science are essential components of success in the Initiative. BRAIN also supports commercialization and dissemination of new instruments through both the Small Business Innovation Research (SBIR) Program, and the BRAIN Initiative Public-Private Partnership Program, and will continue to explore creative opportunities for creating and leveraging trans-NIH and trans-Agency programs. Over the next 1-4 years, the Initiative will disseminate technology through training courses and competitive supplements for NIH-funded investigators to adopt new technologies. Over the next 5-9 years, especially as the type and sophistication of the tools becomes more diverse, the BRAIN Initiative could invest in the establishment of centers with the expertise and facilities that will promote adoption and assist investigators in using new technologies.

iii. *Consider ethical implications of neuroscience research*
The BRAIN Initiative included ethical perspectives in its initial planning and benefited from the advice of the President's Commission for the Study of Bioethical Issues. The MCWG continues to include that perspective, augmented by a standing Neuroethics Division. Consideration of neuroethical implications of BRAIN Initiative research is integral to all activities moving forward. An important component of our strategy is to provide support for research to address and inform ethical issues arising from BRAIN projects.

The NIH Strategic Plan highlights the BRAIN Initiative as an example of its top strategic research objective, advancing biomedical research, and specifically for its focus on fundamental science. BRAIN aims to advance opportunities across neuroscience by dramatically accelerating development of tools and technology.

Supporting the NIH strategic objective to enhance impact through partnerships, NIH has formed the Brain Initiative Alliance with other federal and non-federal participants in the BRAIN Initiative, including the Simons Foundation, Kavli Foundation, Allen Institute for Brain Science, HHMI/Janelia Research Campus, and multiple universities with programs modeled after BRAIN. The members are engaged in the annual BRAIN Initiative Investigator meeting and the NIH BRAIN MCWG. NIH also coordinates funding priorities and addresses neuroethical issues with sister BRAIN Initiative agencies, i.e., National Science Foundation, Defense Advanced Research Projects Agency, Intelligence Advanced Research Project Activity, and the Food and Drug Administration. The NIH BRAIN Initiative Public Private Partnership program works with industry partners to make cutting

edge invasive technologies available to investigators.

In line with NIH Strategic Plan's call to recruit an outstanding workforce, the BRAIN Initiative is bringing scientists from engineering, mathematics, and the physical sciences to neuroscience. In FY 2016 BRAIN funded as many engineers as neuroscientists.

The Strategic Plan call to encourage innovation is central to the BRAIN Initiative, as the tools and technologies developed by BRAIN investigators are already filling major gaps in our current knowledge, and provide unprecedented opportunities for exploring exactly how the brain works. The Initiative includes projects that use cutting-edge technologies to record and modulate brain circuit activity to promote health for conditions such as Parkinson's disease, and recovery from stroke.

III. Cancer Moonshot

A. Overview

The Beau Biden Cancer Moonshot[SM] is an exceptional opportunity to accelerate progress in cancer prevention, diagnosis, treatment, and care. To ensure that the Cancer Moonshot's approaches are grounded in the best science, the National Cancer Institute (NCI) convened a Blue Ribbon Panel (BRP) comprising some of the nation's top cancer experts—cancer researchers, oncologists, patient advocates, and private-sector leaders (see appendix II for BRP roster). The BRP established working groups whose charge was to develop scientific recommendations to meet the goals of the Cancer Moonshot. More than 150 people, including scientists, clinicians, patient advocates, and industry representatives, participated in the working groups. NCI also collected input from the wider research community and the public to supplement the working groups' ideas and ensure reflection of what the broader community viewed as ripe for progress.

In September 2016, the BRP presented its report to the NCI's National Cancer Advisory Board, and the report was approved. The BRP report outlines 10 ambitious but achievable recommendations that shape the scientific blueprint of the Cancer Moonshot. The recommendations represent areas of research that are well-positioned 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:

- 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.
- 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.

Cancer is a complex disease, which is addressed in the BRP report by bringing together the best ideas from science, technology, advocacy, social science, and big data to solve some of cancer's greatest challenges. The Cancer Moonshot builds on the advances made possible by decades of sustained support for cancer research through annual appropriations to the NCI. The specific areas identified as being appropriate for the Moonshot are the direct result of this sustained investment.

B. Innovation Account Funds

The 21st Century Cures Act authorizes the appropriation of $1.8 billion over 7 years "to support cancer research, such as the development of cancer vaccines, the development of more sensitive diagnostic tests for cancer, immunotherapy and the development of combination therapies, and research that has the potential to transform the scientific field,

that has inherently higher risk, and that seeks to address major challenges related to cancer."

Using the Innovation Project funds, NCI intends to initiate a large amount of new research in FY 2017 through FY 2019. Some of the grants will be awarded using multi-year funding authority to provide the necessary flexibility of support for outyear costs and to accelerate the integration, translation, and application of research findings, which will benefit research and patients. Additional efforts to accelerate cancer research will be undertaken through contracts with the cancer community managed through the Frederick National Laboratory for Cancer Research (FNLCR) and other mechanisms. Core research resources at the FNCLR (estimated at <$10M in FY 2017) will also be utilized to underpin Moonshot efforts.

This funding approach will enable NCI to make new grant awards from the Innovation Project funds in every year except for FY 2020 and FY 2021, with most awards being for 5 years. The inability to make new awards in FY 2020 and FY 2021 results from the sharp decrease in funds that starts in FY 2020 (see table below) and ongoing outyear obligations. The current estimated amount of new first year funding for each fiscal year is: $140M in FY 2017, $105M in FY 2018, $60M in FY 2019, none in FY 2020, none in FY 2021, $30M in FY 2022, and $25M in FY 2023.

Funding for Cancer Moonshot Innovation Project under the Cures Act				
Fiscal Year	**Innovation Project Funds**	**Competing**	**Noncompeting**	**Multi year Funded**
2017	$300,000,000	$71,500,000	$15,000,000	$213,500,000
2018	$300,000,000	$90,000,000	$85,000,000	$125,000,000
2019	$400,000,000	$40,000,000	$175,000,000	$185,000,000
2020	$195,000,000	$0	$195,000,000	$0
2021	$195,000,000	$0	$195,000,000	$0
2022	$194,000,000	$40,000,000	$154,000,000	$0
2023	$216,000,000	$5,000,000	$100,000,000	$111,000,000
TOTAL	**$1,800,000,000**	**$246,500,000**	**$919,000,000**	**$634,500,000**

C. Research Categories

Cancer Moonshot activities are comprised primarily of the BRP recommendations, which align with the broad framework authorized by the 21st Century Cures Act and provide a scientific roadmap for the cancer research community to follow to take full advantage of the funding provided through the Innovation Project funds. Estimates will be adjusted based on the quality of applications received. The table below shows a breakdown of funds by category for FY 2017.

Cancer Moonshot Activities	Innovation Funds
Network for Direct Patient Engagement	$18,000,000
Cancer Immunotherapy Translational Science Network	$35,000,000
Therapeutic Target Identification to Overcome Drug Resistance	$27,000,000
Creation of a Data Ecosystem for Sharing and Analysis	$12,000,000
Fusion Oncoproteins in Pediatric Cancer	$10,000,000
Symptom Management Research	$6,000,000
Implementation of Evidence-based Approaches to Prevention	$26,000,000
Retrospective Analysis of Biospecimens from Patients Treated with Standard of Care	$15,000,000
Creation of Human Tumor Atlas	$36,000,000
Technology Development	$44,000,000
Other Cancer Moonshot Priority Activities (e.g., Partnership for Accelerating Cancer Therapies)	$71,000,000

The following are the 10 recommendations outlined in the BRP report and a description of other Cancer Moonshot priority activities:

i. **Network for Direct Patient Engagement ($18M) –** Engage patients to contribute their comprehensive tumor profile data to expand knowledge about what therapies work, in whom, and in which types of cancer.
ii. **Cancer Immunotherapy Translational Science Network ($35M) –** Establish a cancer immunotherapy clinical trials network devoted exclusively to discovering and evaluating immunotherapy approaches for adult and pediatric cancer.
iii. **Therapeutic Target Identification to Overcome Drug Resistance ($27M) –** Identify therapeutic targets to overcome drug resistance through studies that determine the mechanisms that lead cancer cells to become resistant to previously effective treatments.
iv. **Creation of a Data Ecosystem for Sharing and Analysis ($12M) –** Create a national ecosystem for sharing and analyzing cancer data so that researchers, clinicians, and patients will be able to contribute data, which will facilitate efficient data analysis.
v. **Fusion Oncoproteins in Pediatric Cancer ($10M) –** Improve our understanding of fusion oncoproteins in pediatric cancer, and develop new preclinical models and inhibitors that target the fusion oncoproteins.
vi. **Symptom Management Research ($6M) –** Accelerate the development of guidelines for routine monitoring and management of patient-reported symptoms to minimize debilitating side effects of cancer and its treatment.
vii. **Implementation of Evidence-Based Approaches to Prevention ($26M) –** Reduce cancer risk and cancer health disparities through approaches in development, testing, and broad adoption of proven prevention strategies.
viii. **Retrospective Analysis of Biospecimens from Patients Treated with Standard of Care ($15M) –** Predict response to standard treatments

through retrospective analysis of patient specimens.

ix. **Creation of Human Tumor Atlas ($36M) –** Create dynamic 3-D maps of human tumor evolution to document the genetic lesions and cellular interactions of each tumor as it evolves from a precancerous lesion to advanced cancer.

x. **Technology Development ($44M) –** Develop new enabling cancer technologies to characterize tumors and test therapies.

xi. **Other Cancer Moonshot Priority Activities ($71M) –** Additional areas of investment have been identified to transform scientific understanding and address major challenges in cancer prevention, diagnosis, and treatment. NCI, along with its partners in the cancer community, will identify currently intractable problems in cancer science and will support efforts to examine novel insights in these areas, from basic science through translational approaches to clinical trials. For example, through the Partnership for Accelerating Cancer Therapies (PACT), NIH, FDA, biopharmaceutical companies, research foundations, and the Foundation for the NIH are collaborating to identify biomarkers of response to cancer immunotherapies and to prioritize combination therapies for clinical trials. NCI will identify other specific challenges in understanding, preventing, and treating cancer, and use Cures funding to catalyze the research community to address them.

The research activities included in NCI's Cancer Moonshot work plan align directly with the NIH strategic research objective of Advancing Opportunities in Biomedical Research by funding fundamental science research (e.g., creation of the human tumor atlas), treatment and cures research (e.g., cancer immunotherapy translational science network, PACT), and health and promotion of disease prevention research (e.g., symptom management research, implementation of evidence-based approaches to prevention). Moonshot activities indirectly support the other objectives, including Fostering Innovation by Setting NIH Priorities, Enhancing Scientific Stewardship, and Excelling as a Federal Science Agency by Managing for Results.

In FY 2017, NCI is beginning to fund Cancer Moonshot research initiatives aligned with the BRP report. A total of $300M is available in FY 2017 to support initiatives that are advanced enough to enable new research to proceed quickly. Funding is currently obtainable through numerous funding opportunity announcements (FOAs) for research initiatives that address the areas of opportunity identified in the BRP report. The following are some examples:

i. Intensifying research on fusion oncoproteins, which are considered the major drivers of childhood cancers. A better understanding of how oncoproteins function will accelerate development of new therapies that target these cancer- causing proteins in children.

ii. Developing a better understanding of how to unleash a patient's own immune system to fight cancer. Despite some recent successes in immunotherapy, this treatment approach has been effective for some patients only and not always with long-term response. Intensive research is needed so that more adults and children, including those

from underserved populations, can benefit from this approach.

iii. Improving our understanding of how drug resistance develops and finding ways to prevent cancer cells from resisting the drugs meant to kill them. This knowledge can reduce the number of cancer deaths.

iv. Increasing the availability of agents through the NCI Formulary, a public– private partnership between NCI and pharmaceutical and biotechnology companies. This will expedite the start of clinical trials and lead to quicker development of new therapies for patients.

NCI has taken the next step in moving the Cancer Moonshot forward and established 12 implementation teams, with one team for 8 of the 10 BRP recommendations and two teams for the other two recommendations. These teams, comprised of NIH extramural and intramural scientists working in consultation with experts across the country, are charged with identifying research projects that will be evaluated and reviewed by NCI's Board of Scientific Advisors that may be pursued in future fiscal years to realize the opportunities outlined by the BRP. NCI is committed to using Innovation Project funds to support the best science in the community and, where appropriate, to form partnerships with other NIH Institutes and Centers (ICs), as well as foundations, academia, and the private sector to bring about progress for patients. For partnerships between NCI and another NIH IC, NCI has proposed to provide twice as much funding as the other IC.

FY 2017 marks the beginning of a growing Cancer Moonshot portfolio. Planning for longer-term scientific initiatives that will start in future fiscal years is underway within the implementation teams. This will include initiation of BRP recommendations for the network for direct patient engagement and creation of a data ecosystem. NCI will continue to work closely with its advisors and the broad cancer research community to realize the opportunities identified by the BRP and accelerate progress for patient.

IV. Regenerative Medicine

A. Overview

Regenerative medicine (RM) holds the promise to repair or replace cells and tissues damaged by injury, disease, or aging. RM strategies focus on the delivery of therapeutic cells that restore normal structure and function as well as on leveraging and enhancing the body's own innate healing capacity. These strategies include a wide range of technologies such as engineered biomaterials and tissues as well as gene editing or replacement.

Preclinical studies have demonstrated the possibility of these approaches to treat both chronic disease as well as acute injury in a wide range of contexts, and many clinical studies are currently in progress to explore the safety and efficacy of RM therapies. Over the past 25 years, approximately 10 RM therapies (see Appendix III, Table 1) have been approved by the Food and Drug Administration (FDA) for a variety of indications.[3]

Such progress notwithstanding, much work remains to be done to address fundamental gaps in scientific knowledge and overcome technical and operational barriers. Additionally, the prospect of offering definitive RM treatments and cures has given rise to significant "hype" in marketing, including advertising of untested and unapproved regenerative medicine products to patients – underscoring the need for rigorous science and regulatory oversight as well as a national platform for open discussion of the promise and current challenges in the field.[4]

The provision in the Cures Act for a Regenerative Medicine Innovation Project offers an opportunity to galvanize the field and stimulate a comprehensive and coordinated effort to foster major scientific advances and ensure that regenerative medicine clinical studies are standardized, reproducible, and generalizable.

B. Innovation Account Funds

The 21st Century Cures Act authorizes the appropriation of $30 million over 4 years "for clinical research to further the field of regenerative medicine using adult stem cells to further the field of regenerative medicine using adult stem cells, including autologous cells." For this provision, NIH is defining "clinical research" as "Research conducted with human subjects or on material of human origin, such as cells, tissues, and specimens." With respect to the use of "adult stem cells," NIH will only consider research using non-embryonic, non-fetal sources of stem cells to be eligible for these funds.[5]

The Cures Act stipulates that NIH, in coordination with FDA, award grants and contracts "…contingent upon the recipient making available non-Federal contributions…in an amount not less than $1 for each $1 of Federal funds provided in the award" (i.e. a

[3] Mao AS and Mooney DJ. Regenerative medicine: current therapies and future directions. Proceedings of the National Academy of Sciences 112: 14452-14459, 2015

[4] Marks PW, et al. Clarifying stem-cell therapy's benefits and risks. New England Journal of Medicine 376:1007-1009, 2017.

[5] Currently, NIH invests ~$140 million in such clinical research involving non-embryonic, non-fetal sources of stem cells (see Appendix IV; Figure 1) with projects supported by 17 NIH ICs and Offices. The level of NIH investment in this category of RM research has risen by ~30% between FY2011- FY2016, reflecting burgeoning interest in the field.

matching funds requirement). FDA engagement and expertise has been integral to the successful translation of RM strategies from lab bench to clinical care to date; enhanced coordination with FDA will facilitate addressing key regulatory issues in product development and clinical investigation. Successful translation will also be enhanced by private sector engagement in product development, manufacturing, and clinical testing.

As authorized by the Cures Act, the Innovation Project funds are "no-year" funds, meaning that the funds are available until expended. We anticipate that FY 2017 funds ($2 million) will be obligated in the first year with no carry over as these funds will be used to support competitive revisions. In FY 2018 through FY 2020, it is anticipated that a mix of forward funding and regular funding will be used, with a minimum of carry over, as appropriate to each project.

Funding for Regenerative Medicine Innovation Project under the Cures Act			
Fiscal Year	**Innovation Project Funds**	**Total Funds w/Matching**	**Description**
2017	$2,000,000	$4,000,000	• A Notice of Intent to Publish will be issued as soon as possible to alert the scientific community that applications will be sought for competitive revisions in FY 2017 and for project grants in FYs 2018-20 and to make them aware of the matching requirement • Utilize competitive revisions to fund significant new opportunities leveraging extant projects • Applications for supplemental funds to be solicited through a Funding Opportunity Announcement that includes a cash or in- kind matching funds requirement • Applications to be reviewed by NIH in coordination with FDA, followed by secondary review by Council
2018	$10,000,000	$20,000,000	Solicitation of projects with a cash or in-kind matching requirement; scientific scope of the FOA will be informed by expert consultation
2019	$10,000,000	$20,000,000	Solicitation of projects with a cash or in-kind matching requirement; scientific scope of the FOA will be informed by workshop consultation
2020	$8,000,000	$16,000,000	Solicitation of projects with a cash or in-kind matching requirement; scientific scope of the FOA will be informed by workshop consultation
Total s	**$30,000,000**	**$60,000,000**	

C. Research Categories

For the RM Innovation Project, NIH will both support specific research projects and stimulate the development of a sustainable foundation for the future of the field. The work plan focuses on two components:

i. **Identification of highly meritorious clinical research projects** that are well poised to put Innovation Project funds to best use in exploring and enabling the development of safe and RM interventions. Specifically, for FY 2017 funds, in

addition to being reviewed under the standard NIH review criteria, clinical research projects will also be assessed according to the following specific criteria, consistent with the NIH peer review standards, as well as funding priorities and procedural and programmatic considerations:

a. Represents unfunded opportunities (can put funds to new and immediate use)
b. Underlying project is well along/already underway
c. Matching funds available at time of award
d. Contributes to breadth/diversity of RM science
e. Addresses a critical knowledge gap and/or technical barrier
f. Will help to significantly build or advance the field of RM
g. Contributes to regulatory science in RM (e.g., quality control, data standards)

Such projects will be solicited through FOAs that will set forth the matching requirement. The applications will be reviewed by a Special Emphasis Panel (and in coordination with FDA) and referred to Council for secondary review in September 2017. Solicitations for applications in FYs 2018-20 will be informed by the consultations and activities as described below. Of note, a Notice of Intent to Publish (NOITP) will be issued prior to the first FOA and will announce the planned solicitation for competitive revisions in FY 2017 as well as for new Investigator- initiated projects in FY 2018 and beyond. The NOITP will also provide advance notice of the matching fund requirement.

ii. **Catalyzing sustained and accelerated development of the field** through enabling the critical foundation and infrastructure for product development, clinical testing, and data standards and sharing, including:

a. Better and shared understanding of current technical and operational barriers as well as the regulatory science issues
b. Further development of standards and Good Manufacturing Practice for adult stem cell-based RM products (e.g., Dental, Oral, and Craniofacial Tissue Regeneration Consortium)
c. Leveraging extant cell production facilities for product preparation and qualification (e.g., Production Assistance for Cellular Therapies, NIH Clinical Center cell production facility)
d. Promoting and enhancing mechanisms for data standardization, curation, integration, and sharing (e.g., FaceBase)
e. Utilization of clinical trial network(s) to leverage infrastructure and facilitate subject recruitment and follow up as well as data sharing (e.g., Cardiovascular Cell Therapy Research Network, Clinical Islet Transplantation (CIT) Consortium**,** Hematopoietic Stem Cell Therapy Consortium, Clinical Trials in Organ Transplantation, Immune Tolerance Network, Autoimmunity Centers of Excellence)

To identify the scientific areas poised for major transformative advances as well as the critical gaps that must be addressed to enable significant innovation and rapid advancement of the field, NIH plans to convene a multi-disciplinary, multi-sector **Roundtable Workshop** in fall 2017. The workshop will explore the specific issues related to product development, regulatory science, and clinical applications and inform the specific future

directions and refinement of the Innovation Project. Involvement of FDA as well as engagement of the private sector and research community will be critical the workshop's design and outputs. The design of the workshop will also take into account other public consultations and assessments of the state of the science.[6] A major goal of this workshop will be to inform the development of an overarching **Regenerative Medicine Innovation Blueprint** to help stimulate major transformative rather than incremental progress in the field. The Blueprint will be refined through additional internal and external consultations, including with NIH scientific program staff and leadership, FDA scientists and leadership, the NIH Advisory Committee to the Director, as well as the private sector, research community, and the general public.

To guide NIH's implementation of the RM Innovation Project, the Agency has established two groups:

i. **A Working Group of RM Subject Matter Experts** from across NIH to:
    a. provide input on criteria that could be used in the development and review of RM research proposals
    b. assist in the development of a draft solicitation for supplemental funding applications from the research community
    c. participate in the review of applications
    d. identify options to implement the RM Innovation Project in FYs 2018-20
    e. provide options and recommendations to the Innovation Project Oversight Committee as needed, including for the design of the Roundtable Workshop and the development of the RM Innovation Blueprint

ii. **A RM Innovation Project Oversight Committee** to advise the NIH Director on utilization of the RM Innovation Project funds. The Committee will be chaired by an Institute Director appointed by the NIH Director to act on his behalf. Final decisions about utilization of RM Innovation funds will be made by the NIH Director. In addition to chair, the Committee will be comprised of senior leadership from relevant NIH ICs and OD. Key activities may include, but are not limited to:
    a. conceptualizing the critical elements of an RM "blueprint" (e.g., infrastructure, data standards, reference cell lines)
    b. identifying potential synergies with other relevant scientific initiatives
    c. coordinating with FDA on regulatory science needs, patient safety, and public trust with respect to RM use of adult stem cells
    d. facilitating and overseeing the solicitation, merit review, and Council review of applications for Innovation Project funds

NIH's support of and investment in RM research using the Innovation Project funds supports several key strategic research priorities in NIH-Wide Strategic Plan. One priority is to advance opportunities in biomedical research by fostering fundamental science and facilitating the development of treatments and cures. For treatments and cures, the Strategic Plan identifies particularly promising areas of RM research worthy of investment because

[6] Markowitz-Shulman A, et al. Exploring the state of the science in the field of Regenerative Medicine: Challenges of and opportunities for cellular therapies (Proceedings of a Workshop). *National Academies of Sciences Report*, 2017

of their therapeutic potential. Other strategic priorities are innovation and collaboration with Federal and private sector partners with an eye toward accelerating the development of treatments and cures. NIH will work closely with FDA in implementing the Cures Act to address this regulatory science question and find opportunities to accelerate the product approval process. The non-federal funding matching requirement provides additional impetus for the public-private partnerships that are encouraged under the Strategic Plan.

Appendix I: Relevant 21st Century Cures Act Language

Section 1001(c) of the 21st Century Cures Act
P.L. 114-255

(c) Accountability And Oversight.—

(1) WORK PLAN.—

(A) IN GENERAL.—Not later than 180 days after the date of enactment of this Act, the Director of NIH shall submit to the Committee on Health, Education, Labor, and Pensions and the Committee on Appropriations of the Senate and the Committee on Energy and Commerce and the Committee on Appropriations of the House of Representatives, a work plan including the proposed allocation of funds authorized to be appropriated pursuant to subsection (b)(3) for each of fiscal years 2017 through 2026 for the NIH Innovation Projects and the contents described in subparagraph (B).

(B) CONTENTS.—The work plan submitted under subparagraph (A) shall include—

(i) recommendations from the Advisory Committee described in subparagraph (C);

(ii) the amount of money to be obligated or expended in each fiscal year for each NIH Innovation Project;

(iii) a description and justification of each such project; and

(iv) a description of how each such project supports the strategic research priorities identified in the NIH Strategic Plan under subsection (m) of section 402 of the Public Health Service Act (42 U.S.C. 282), as added by section 2031.

(C) RECOMMENDATIONS.—Prior to submitting the work plan under this paragraph, the Director of NIH shall seek recommendations from the Advisory Committee to the Director of NIH appointed under section 222 of the Public Health Service Act (42 U.S.C. 217a) on—

(i) the allocations of funds appropriated pursuant to the authorization of appropriations under subsection (b)(3) for each of fiscal years 2017 through 2026; and

(ii) on the contents of the proposed work plan.

Appendix II: Cancer Moonshot Blue Ribbon Panel

The Cancer Moonshot Blue Ribbon Panel was composed of leading experts from a broad range of scientific areas, including biology, immunology, genomics, diagnostics, bioinformatics, and cancer prevention and treatment. Members also included investigators with expertise in clinical trials and cancer health disparities, as well as representatives of cancer advocacy groups and pharmaceutical and biotechnology companies.

The members of the Blue Ribbon Panel were:

Tyler Jacks, Ph.D. (Co-Chair)
Chair, National Cancer Advisory Board
Director, Koch Institute for Integrative Cancer Research, Massachusetts Institute of Technology

Elizabeth Jaffee, M.D. (Co-Chair)
Professor and Deputy Director for Translational Research, Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University School of Medicine

Dinah Singer, Ph.D. (Co-Chair and Designated Federal Official)
Acting Deputy Director, National Cancer Institute
Director, Division of Cancer Biology, National Cancer Institute

Peter Adamson, M.D.
Professor and Director, Experimental Therapeutics in Oncology, The Children's Hospital of Philadelphia

James Allison, Ph.D.
Professor and Chair of Immunology, University of Texas MD Anderson Cancer Center

David Arons, J.D.
Chief Executive Officer, National Brain Tumor Society

Mary Beckerle, Ph.D.
Chief Executive Officer and Director, Huntsman Cancer Institute, University of Utah

Mitch Berger, M.D.
Professor and Chair, Department of Neurological Surgery, University of California, San Francisco

Jeff Bluestone, Ph.D.
A.W. and Mary Margaret Clausen Distinguished Professor of Metabolism and Endocrinology, University of California, San Francisco

Chi Van Dang, M.D., Ph.D.
Professor of Medicine and Director, Abramson Cancer Center, University of Pennsylvania

Mikael Dolsten, M.D., Ph.D.
President, Pfizer Worldwide Research and Development
Executive Vice President, Pfizer, Inc.

James Downing, M.D.
President and Chief Executive Officer, St. Jude Children's Research Hospital

Levi Garraway, M.D., Ph.D.
Associate Professor of Medicine, Harvard Medical School
Assistant Professor of Medicine, Dana-Farber Cancer Institute

Gad Getz, Ph.D.
Director of Cancer Genome Computational Analysis Group and Institute Member, Broad Institute of MIT and Harvard
Director, Bioinformatics Program, Massachusetts General Hospital Cancer Center and Department of Pathology
Associate Professor of Pathology, Harvard Medical School
Paul C. Zamecnik Chair in Oncology, MGH Cancer Center

Laurie Glimcher, M.D.
Professor of Medicine and Stephen and Suzanne Weiss Dean, Weill Cornell Medical College
Incoming President and Chief Executive Officer, Dana-Farber Cancer Institute

Lifang Hou, M.D., Ph.D.
Associate Professor of Preventive Medicine, Robert H. Lurie Comprehensive Cancer Center, Northwestern University Feinberg School of Medicine

Neal Kassell, M.D.
Chairman, Focused Ultrasound Foundation
Professor of Neurosurgery, University of Virginia

María Elena Martínez, Ph.D.
Sam M. Walton Endowed Chair for Cancer Research, Professor of Family Medicine and Public Health, and Co-director of the Reducing Cancer Disparities Program, UC San Diego Moores Cancer Center

Deborah Mayer, Ph.D., R.N.
Professor of Adult and Geriatric Health, University of North Carolina School of Nursing
Director of Cancer Survivorship, UNC Lineberger Comprehensive Cancer Center

Edith Mitchell, M.D., F.A.C.P
Professor of Medical Oncology and Associate Director for Diversity Services, Sidney Kimmel Cancer Center at Thomas Jefferson University

Augusto Ochoa, M.D.
Professor of Pediatrics and Director, Stanley S. Scott Cancer Center, Louisiana State University

Jennifer Pietenpol, Ph.D.
Benjamin F. Byrd, Jr. Professor of Oncology, Professor of Biochemistry, and Director, Vanderbilt-Ingram Cancer Center

Angel Pizarro, M.S.E.
Technical Business Development Manager, Amazon Web Services Scientific Computing and Research Computing

Barbara Rimer, Dr.P.H.
Alumni Distinguished Professor and Dean, University of North Carolina Gillings School of Global Public Health

Charles Sawyers, M.D.
Chair, Human Oncology and Pathogenesis Program, Memorial Sloan Kettering Cancer Center
Investigator, Howard Hughes Medical Institute

Ellen Sigal, Ph.D.
Founder and Chair, Friends of Cancer Research

Patrick Soon-Shiong, M.D., FRCS (C), FACS
Founder, Chair, and CEO, NantWorks LLC

Wai-Kwan Alfred Yung, M.D.
Professor of Neuro-Oncology and Chair of Clinical Cancer Care, University of Texas MD Anderson Cancer Center

Ex Officio members of the Blue Ribbon Panel were:

David Atkins, M.D., M.P.H.
Acting Chief Research and Development Officer, Department of Veterans Affairs

Robert Califf, M.D.
Commissioner, U.S. Food and Drug Administration

Karen Guice, M.D., M.P.P.
Acting Assistant Secretary of Defense for Health Affairs, Department of Defense

Jason Paragas, Ph.D.
Director of Innovation, Lawrence Livermore National Laboratory

Lawrence Tabak, D.D.S., Ph.D.
Principal Deputy Director, National Institutes of Health

Appendix III: Regenerative Medicine Products Approved by the FDA

Category	Name	Biological agent	Approved use
Biologics	laViv	Autologous fibroblasts	Improving nasolabial fold appearance
	Carticel	Autologous chondrocytes	Cartilage defects from acute or repetitive trauma
	Apligraf, GINTUIT	Allogeneic cultured keratinocytes and fibroblasts in bovine collagen	Topical mucogingival conditions, leg and diabetic foot ulcers
	Cord blood	Hematopoietic stem and progenitor cells	Hematopoietic and immunological reconstitution after myeloablative treatment
Cell-based medical devices	Dermagraft	Allogenic fibroblasts	Diabetic foot ulcer
	Celution	Cell extraction	Transfer of autologous adipose stem cells
Biopharmaceuticals	GEM 125	PDGF-BB, tricalcium phosphate	Periodontal defects
	Regranex	PDGF-BB	Lower extremity diabetic ulcers
	Infuse, Infuse Bone Graft, Inductos	BMP-2	Tibia fracture and nonunion, and lower spine fusion
	Osteogenic protein-1	BMP-7	Tibia nonunion

Source: Mao AS and Mooney DJ. Regenerative medicine: Current therapies and future directions.
Proceedings of the National Academy of Sciences 112: 14452–14459, 2015

Appendix IV: Regenerative Medicine Human Subjects Research at NIH

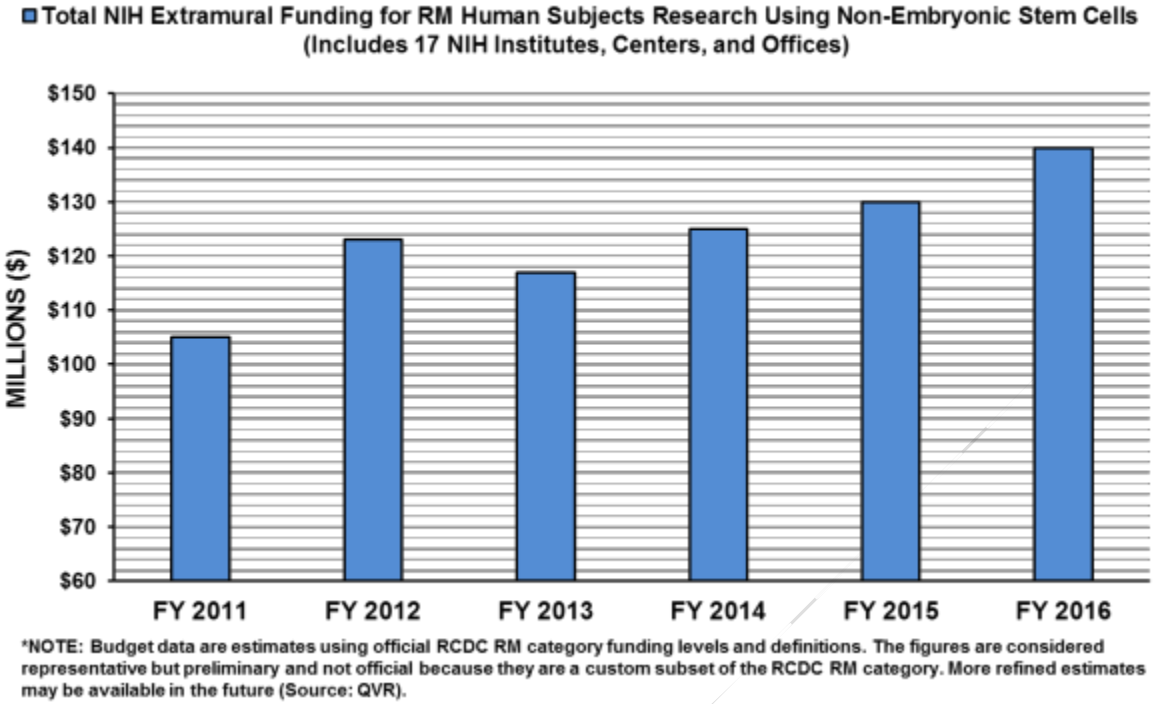

*Figure showing total funding for NIH awards belonging to RCDC category 'Regenerative Medicine' Human Subjects Research Using Non-Embryonic Stem Cells for FY11-FY16.**