DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

Fiscal Year 2016 Budget Request

Witness appearing before the

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Good morning, Chairman Blunt, Ranking Member Murray, and distinguished Members of the Subcommittee. I am Francis S. Collins, M.D., Ph.D., and I am the Director of the National Institutes of Health (NIH). It is an honor to appear before you today to present the Administration's fiscal year (FY) 2016 budget request for the NIH, and provide an overview of our central role in enhancing the nation's health through scientific discovery.

As the nation's premier biomedical research agency, NIH's mission is to seek fundamental knowledge about the nature and behavior of living systems, and to apply that knowledge to enhance human health, lengthen life, and reduce illness and disability. I can report to you today that NIH leadership, employees, and grantees continue to believe passionately in that mission.

As a federal research agency, we are also acutely aware that in order to achieve our mission we must serve as effective and efficient stewards of the resources we have been given by the American public. One way in which we are accomplishing this is by focusing intensively on prioritization of NIH resources. This involves developing and applying advanced methods of portfolio analysis, identifying the most compelling scientific opportunities within each Institute and Center, fostering creative trans-NIH collaborations, and enhancing use of the Common Fund. We are also implementing novel external partnerships like the NIH-DARPA-FDA project on a human biochip for testing drug toxicity, and the Accelerating Medicines Partnership with ten pharmaceutical companies to develop the next generation of drug targets for Alzheimer's disease, type 2 diabetes, rheumatoid arthritis, and lupus. To support this focus on priority setting, we are developing an overarching NIH strategic plan, and will be linking this with individual Institute/Center (IC) strategic plans that reflect the rapid current progress in bioscience. We are also working to optimize the peer review process to enhance diversity, fairness, and the rigor and reproducibility of NIH-supported science. And finally, we remain 100 percent committed to strengthening and sustaining our most important resource, the scientists who do this critical work, by

incentivizing early stage young investigators, revitalizing physician-scientist training, and increasing the diversity of our research workforce. With these goals in mind, we are confident we will be able to support the best and brightest ideas, while maintaining our core mission and inspiring public trust in the world's premier biomedical research agency.

NIH has been advancing the understanding of health and disease for more than a century, and many of our contributions stem from our nation's commitment to investing in basic science research. Basic science lays the foundation for advances in disease diagnosis, treatment, and prevention by providing the building blocks for clinical applications. Basic science is generally not supported in the private sector, and NIH's focus on understanding fundamental biological processes fosters innovation and ultimately leads to effective ways to treat complex medical conditions. Our successful investment in basic science is reflected by the awarding of no less than 145 Nobel prizes to NIH-supported scientists; the vast majority of these individuals were recognized for basic science advances.

A compelling current example of how basic science is revolutionizing the future of biomedical research is in a potential treatment for the deadly Ebola virus. The experimental Ebola treatment, ZMapp, received a lot of attention last summer when it was shown to provide protection in a non-human primate model, but was in very short supply and had never been rigorously tested in humans. ZMapp is a cocktail of three monoclonal antibodies directed against the coat protein of the virus. But it's important to know where those antibodies actually bind to the protein, and how that would interfere with Ebola's ability to infect cells. NIH-supported researchers at The Scripps Research Institute in California set out to answer these questions. Using a high-resolution imaging technique called single-particle electron microscopy, the researchers recently mapped in exquisite three-dimensional detail the binding of the

ZMapp antibodies on the surface of the Ebola virus.[1] The images revealed that two of the three antibodies work by neutralizing the virus, by preventing it from attaching to and fusing into the host cell, while the third antibody acts as a beacon, alerting the host immune system that the virus has invaded and must be destroyed. Not only has this elegant experiment in basic structural biology provided the scientific rationale for ZMapp as an effective Ebola treatment – something we are actively testing in clinical trials – it also provides key information for the development of additional therapies for this rapidly mutating virus. Moreover, it illustrates the power of this three-dimensional imaging technique to identify targets for future drugs and vaccines.

Another way we are trying to unravel life's mysteries through basic science is with the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative—and we are grateful to this subcommittee for its FY2014 and FY 2015 support, and hope to ramp this up further in FY 2016. This bold, multi-agency effort to revolutionize our understanding of the human brain will enable the development and use of innovative technologies to produce a clearer, more dynamic picture of how individual cells and neural circuits interact in both time and space. By measuring activity at the scale of neural networks in living organisms, we can begin to decode sensory experience and, potentially, even memory, emotion, and thought. Ultimately, the technologies developed under the BRAIN Initiative may help reveal the underlying pathology in a vast array of brain disorders and provide new therapeutic avenues to treat, cure, and prevent neurological and psychiatric conditions such as Alzheimer's disease, autism, schizophrenia, epilepsy, traumatic brain injury, and addiction.

Scientific advances are also accelerating progress toward a new era of personalized medicine. Historically, physicians have had to make most recommendations about disease prevention and treatment based on the expected response of the average patient. This one-size-fits-all approach works

[1] Structures of protective antibodies reveal sites of vulnerability on Ebola virus. Murin CD, Fusco ML, Bornholdt ZA, Qiu X, Olinger GG, Zeitlin L, Kobinger GP, Ward AB, Saphire EO. *Proceedings of the National Academies of Sciences*. 2014 Nov 17.

for some patients and some conditions, but not others. Technology developments, along with plummeting costs of DNA sequencing, now make it possible to develop an innovative approach to treatment that accounts for individual differences in patients' genes, environments, and lifestyles. With this in mind, we are excited to take a lead role in the multi-agency Precision Medicine Initiative (PMI). A near term goal of the PMI focuses on cancer; cancer research has been leading the way in precision medicine for many years, by defining the driver mutations in individual tumors and using this information to design the ideal therapy for each patient. To accelerate the pace of demonstrating clinical benefits, this initiative seeks to expand current cancer genomics research to understand the development of resistance to targeted therapy, to apply non-invasive methods to track patients' responses to treatment, and to explore the efficacy of new drug combinations targeted to specific tumor mutations.

As a longer term goal of this initiative, NIH will also launch a national research cohort of one million or more volunteers who will play an active role in how their genetic, environmental, and medical information is used for the prevention of illness and management of a wide array of chronic diseases. The goal will be to expand the benefits of precision medicine into myriad aspects of health and health care. Voluntary participants will share clinical data from electronic health records, results of imaging and laboratory tests, lifestyle data and environmental exposure recordings tracked through real time mobile health devices, and genomic information. Participants will be at the center of the project design, and they will have access to their own health data, as well as research using their data, to help inform their own health decisions. Through this dynamic community, researchers will be able to advance the information derived from this cohort into new knowledge, approaches, and treatments. A project of this magnitude will lay the foundation for a myriad of new prevention strategies and novel therapeutics. There's no better time than now to embark on this ambitious new enterprise to revolutionize medicine

and generate the scientific evidence necessary to move this individualized approach into everyday clinical practice.

Another way we are turning discovery into health is in our efforts to combat the problem of Antimicrobial Resistance (AMR). Because most bacteria, viruses, and other microbes multiply rapidly in a short period of time, they can evolve and develop resistance to antimicrobial drugs. Public health surveillance has documented an alarming increase in AMR, especially those strains that cause hospital-acquired infections. Each year in the United States, more than two million people acquire serious infections from bacteria that are resistant to antibiotics designed to treat those infections, and approximately 23,000 of these people die. Recognizing the growing public health threat of AMR, NIH is engaged in the Administration's National Plan to Combat Antibiotic Resistant-Bacteria—a multi-agency venture, in collaboration with the U.S. Food and Drug Administration, the U.S. Department of Agriculture, and the Centers for Disease Control and Prevention, designed to reverse these disturbing trends. To this end, we will expand efforts to develop new antibiotics, like the teixobactin recently identified by an NIH grantee that shows great promise against the difficult-to-treat infections, methicillin-resistant Staphylococcus aureus (MRSA) and resistant tuberculosis. We will work to develop a rapid diagnostic test for resistant organisms that will be of critical clinical and public health utility. With this goal in mind, the National Institute of Allergy and Infectious Diseases recently awarded funding for nine research projects supporting enhanced diagnostics to rapidly detect antimicrobial-resistant bacteria. We will also build a national genome sequence database on all reported resistant human infections. And we will create a rapid response clinical trial network that is ready to test new antibiotics on individuals infected with highly resistant strains of bacteria.

Preventing disease has always been a top priority for NIH, and influenza is one area of prevention in which we are poised for significant progress. Currently, to provide protection against the

rapidly evolving influenza virus, a new vaccine must be produced each year. Despite our best efforts, some guesswork is involved, and the vaccine isn't always ideal—as we know all too well after this particularly difficult flu season. In an average year, the flu claims up to 49,000 American lives and costs the U.S. economy about $87 billion. But it does not have to be that way. NIH-funded researchers continue to move forward on a universal flu vaccine—designed to produce broad protection against virtually all strains of the flu for extended periods of time and, thus, potentially reduce the need for annual flu shots and the risk of a global pandemic. I am happy to report that universal flu vaccine candidates have now moved into early stage clinical trials.

So far, I've described for you several examples of NIH's commitment to basic, translational, and clinical research. But, none of this would be possible without a diverse and talented biomedical workforce. Recruiting and retaining the brightest minds regardless of race, ethnicity, gender, disability, and socioeconomic status is critically important not only to NIH, but to the entire American scientific enterprise. That is why we are taking new and aggressive steps to attract the most talented individuals from all groups. The BUilding Infrastructure Leading to Diversity (BUILD) Initiative is a bold experiment, consisting of a set of training awards designed to attract a diverse array of students into the training pipeline and encourage their futures as NIH-supported researchers. In addition to BUILD, we also established the National Research Mentoring Network (NRMN). The network establishes a nationwide, interconnected set of skilled mentors linked to mentees from a variety of scientific and social backgrounds. These efforts should strongly support our goal to enhance the diversity and maximize the talent of the biomedical workforce.

While all of these exciting research efforts and scientific opportunities are leading to a much deeper understanding of health and human disease, much more work needs to be done. The NIH has lost approximately 22 percent of its purchasing power for research since 2003, and the likelihood that a

grant applicant will achieve funding after peer review has fallen to the lowest in decades, now less than 20 percent. Other countries are expanding their support for medical research. To put NIH back on an increasingly stable trajectory, the President's FY 2016 budget request for the NIH is $31.311 billion, $1 billion or 3.3 percent above the enacted FY 2015 level. This budget request reflects the President's and the Secretary's commitment to improving the health of the nation and to maintaining our nation's leadership in the life sciences. The request highlights investments in innovative research that will advance fundamental knowledge, and speed the development of new therapies, diagnostics, and preventive measures to improve public health, including $200 million for the Precision Medicine Initiative and an additional $100 million to combat AMR.

The FY 2016 budget request will enhance NIH's ability to support cutting-edge research and training of the scientific workforce. Within this budget, we will increase Research Project Grants (RPGs), NIH's funding mechanism for investigator-initiated research. NIH expects to support 10,303 new and competing RPGs in FY 2016, an increase of 1,227 above the FY 2015 estimate. The budget request allocates resources to areas of the most extraordinary promise for biomedical research, while maintaining the flexibility to pursue unplanned scientific opportunities and address unforeseen public health needs.

I have provided you with examples of how investments in biomedical research through NIH are advancing human health, spurring innovations in science and technology, stimulating economic growth, and laying the groundwork for the future of the United States biomedical research enterprise. We have never witnessed a time of greater promise for advances in medicine than right now. With your support, the future of medicine can be very bright.

This concludes my testimony, and I look forward to answering your questions.