

**PREPARED STATEMENT OF CHRISTOPHER P. AUSTIN, M.D.
DIRECTOR,
NATIONAL CENTER FOR ADVANCING TRANSLATIONAL SCIENCES**

Mr. Chairman and Members of the Committee: I am pleased to present the President's Fiscal Year (FY) 2019 budget request for the National Center for Advancing Translational Sciences (NCATS) of the National Institutes of Health.

NCATS is dedicated to understanding and transforming *translation*, defined as the process of turning scientific, medical, and public health observations in the laboratory, clinic, and community into interventions that improve the health of individuals and the public. At a time of unprecedented science discoveries, our collective ability to translate research findings into health benefits often is too slow and ineffective. Developing a new drug requires on average 10 to 15 years and more than \$2 billion given the high prevalence of failure along the translational pipeline. We must deliver the promise of science to patients in an accelerated and more efficient manner. NCATS studies and supports translation on a system-wide level as a scientific and operational problem, addressing roadblocks that impede or preclude promising advances.

Accelerating Clinical Translation

The largest portion of NCATS' budget is dedicated to its Clinical and Translational Science Awards (CTSA) Program. Through this program, NCATS supports a national network of medical research centers, called hubs, that collaborate locally, regionally, and nationally to foster innovation in clinical researcher training, patient engagement, and new research tools and processes. There are multiple initiatives within this program, including the Trial Innovation Network that is composed of the hubs as well as Trial Innovation Centers and a Recruitment Innovation Center. Through this network, researchers are identifying and implementing ways to improve the clinical trial process, including participant recruitment and other aspects of clinical trial conduct.

The process of obtaining ethics approval from multiple institutional review boards (IRBs) to conduct a clinical research study at multiple institutions is a longstanding challenge that can lead to significant delays in study activation. To address this problem, NCATS supported the development of a single IRB reliance platform for multisite clinical studies, enabling study sites to rely on a single IRB of record. The platform, known as the Streamlined, Multisite, Accelerated Resources for Trials (SMART) IRB, includes resources such as umbrella agreements, guidance documents, and consultation services that investigators nationwide can access to harmonize and streamline IRB review for their own multisite studies. SMART IRB is serving as a roadmap to help implement the NIH policy released in June 2016 that requires all NIH-funded multisite clinical studies to use a single IRB.

Providing the resources to train, cultivate, and sustain future leaders of the biomedical research workforce is another key CTSA Program emphasis. The program supports a coordinated, national effort to help ensure a pipeline of trained translational investigators who can move basic research findings into applications for improving health outcomes as novel

therapies, diagnostics, and preventives. Program grantees have developed clinical and translational sciences training resources, including educational core competencies, best practices for training mentors, and curriculum materials. These tools are freely available, and many institutions nationwide are using them.

Engaging patients at all stages of translation is crucial; their perspectives as members of the research team provide insights, focus, urgency and connectivity that can be instrumental in making the development, testing and deployment of new interventions more effective. NCATS supports the Rare Diseases Clinical Research Network (RDCRN) and requires each consortia member to include patient groups as full partners on their research teams, an approach that helps achieve greater success. The RDCRN Coalition of Patient Advocacy Groups develops and shares best practices, and the RDCRN website includes a contact registry for patients who may be interested in participating in RDCRN clinical studies. Rare diseases, which cumulatively affect approximately one in 10 people in the U.S., are in crucial need of innovative translational technologies, and are thus a crucial NCATS focus.

Measurable outcomes can help determine whether a new translational process is actually an improvement. NCATS' Discovering New Therapeutic Uses for Existing Molecules program matches academic investigators with pharmaceutical companies that have compounds that were found to be ineffective in treating specific diseases. Repurposing these compounds for potentially treating other diseases saves time in the drug development process because significant foundational work already has been completed. NCATS helps to further accelerate this process by providing collaboration agreement templates that now are being used broadly in the research community and by supporting researchers with new ideas for how existing compounds can be repurposed.

Finding New Therapies for Clinical Study

NCATS also is dedicated to removing pre-clinical translational science roadblocks. Through its Therapeutics for Rare and Neglected Diseases (TRND) program, the Center works to “de-risk” potential therapeutics so that private sector companies may be more inclined to acquire them to finish their development.

Despite promising results in clinical trials outside of the U.S., work on further developing a gene therapy for the rare pediatric disease aromatic L-amino acid decarboxylase (AADC) deficiency was seemingly insurmountable. Through TRND, NCATS teamed with a private sector partner, Agilis Biotherapeutics, to convert promise into reality, jointly creating a manufacturing process for a therapy that complies with FDA regulations, and obtaining the required pre-clinical data. In addition to getting this potentially lifesaving therapy to patients, this project established technological and regulatory models that will accelerate development of other rare disease gene therapies.

The NCATS Cures Acceleration Network (CAN) supports high-risk, innovative programs to advance the development of high-need cures and reduce significant barriers between research discovery and clinical trials. Through the CAN-funded Tissue Chip for Drug Screening program, NCATS is working on new methods for predicting both safety and efficacy of

experimental drugs using engineered “chips” that contain human cells and model human organs. Current methods such as animal and cell models are not always reliably predictive and can result in wasted time and effort. In addition to developing these chips for testing potential drugs, NCATS soon will send tissue chips to the International Space Station (ISS) for research on the effect of microgravity on these model organs. Microgravity can accelerate aging and have other effects relevant to diseases on Earth, making the ISS a unique and significant research environment.

New drug development for currently untreatable diseases has been greatly limited because known chemical structures affect only 10 percent of potential drug targets within the human body. With CAN support, NCATS plans to launch its Automated Synthesis Platform for Innovative Research and Execution (ASPIRE) program to bring together chemistry, robotic engineering, biological activity testing, and artificial intelligence. Tools developed through ASPIRE will minimize the time chemists spend on tedious and repetitive tasks, freeing them up for more complicated pursuits such as designing, synthesizing, and testing compounds for diseases that currently have no treatment.

Adaptability to Tackle Emerging Public Health Needs

With its unique collection of programs, initiatives and resources, NCATS has the capacity and capability to address public health crises. For example, a team of researchers from NCATS and the Icahn School of Medicine at Mount Sinai developed a miniaturized assay for high-throughput screening to find compounds that block the ability of Ebola virus-like particles (VLPs) to enter and infect cells. A screen using 2,816 compounds identified 53 drugs with entry-blocking activity against Ebola VLPs.

In another example, investigators from Johns Hopkins University and Florida State University collaborated with NCATS experts on drug repurposing and high throughput screening to identify rapidly two classes of existing compounds that potentially can be used to fight Zika. These compounds were effective either in inhibiting the replication of the Zika virus or in preventing the virus from killing brain cells. All data have been made available through public databases, allowing these compounds to be further studied by the broader research community.

NCATS also is well-positioned to help combat the current national epidemic of opioid abuse. The Center’s high-throughput screening facility could be used to test potential opioid abuse therapeutics, and CTSA Program-supported researchers could help identify opioid patients and rapidly enroll them in multisite clinical trials.

Conclusion

Through its programs and initiatives described above, and others, NCATS is improving health through smarter science in unprecedented ways, with the ultimate goal of getting more treatments to more patients — and to the public at large — more quickly.

Christopher P. Austin, M.D.
Director, National Center for Advancing Translational Sciences

Dr. Austin leads NCATS' work to improve the translation of observations in the laboratory, clinic and community into interventions that reach and benefit patients—from diagnostics and therapeutics to medical procedures and behavioral changes. Under his direction, NCATS researchers and collaborators are developing new technologies, resources and collaborative research models; demonstrating their usefulness; and disseminating the data, analysis and methodologies for use by the worldwide research community.

Dr. Austin's career has spanned the spectrum of translational research, in the public and private sectors. Dr. Austin joined NIH in 2002 as the senior advisor to the director for translational research at the National Human Genome Research Institute, where he was responsible for conceptualizing and implementing research programs to derive scientific insights and therapeutic benefit from the newly completed Human Genome Project. While at NHGRI, he founded and directed the NIH Chemical Genomics Center, Therapeutics for Rare and Neglected Diseases program, Toxicology in the 21st Century initiative, and NIH Center for Translational Therapeutics. Upon the creation of NCATS in 2011, he became the inaugural director of the NCATS Division of Pre-Clinical Innovation and was appointed NCATS director in 2012. In 2016, Dr. Austin was elected chair of the International Rare Disease Research Consortium (IRDIRC). Prior to joining NIH, Dr. Austin worked at the pharmaceutical company Merck, where he directed programs on genome-based discovery of novel targets and drugs, with a particular focus on schizophrenia and Alzheimer's disease.

Dr. Austin is trained as a clinician and geneticist. He trained in internal medicine and neurology at the Massachusetts General Hospital in Boston and practiced medicine in academic and community hospital settings as well as in urban primary care and in rural Alaska and Africa. He completed a research fellowship in developmental neurogenetics at Harvard, studying genetic and environmental influences on stem cell fate determination. Dr. Austin earned an M.D. from Harvard Medical School and A.B. *summa cum laude* in biology from Princeton University.