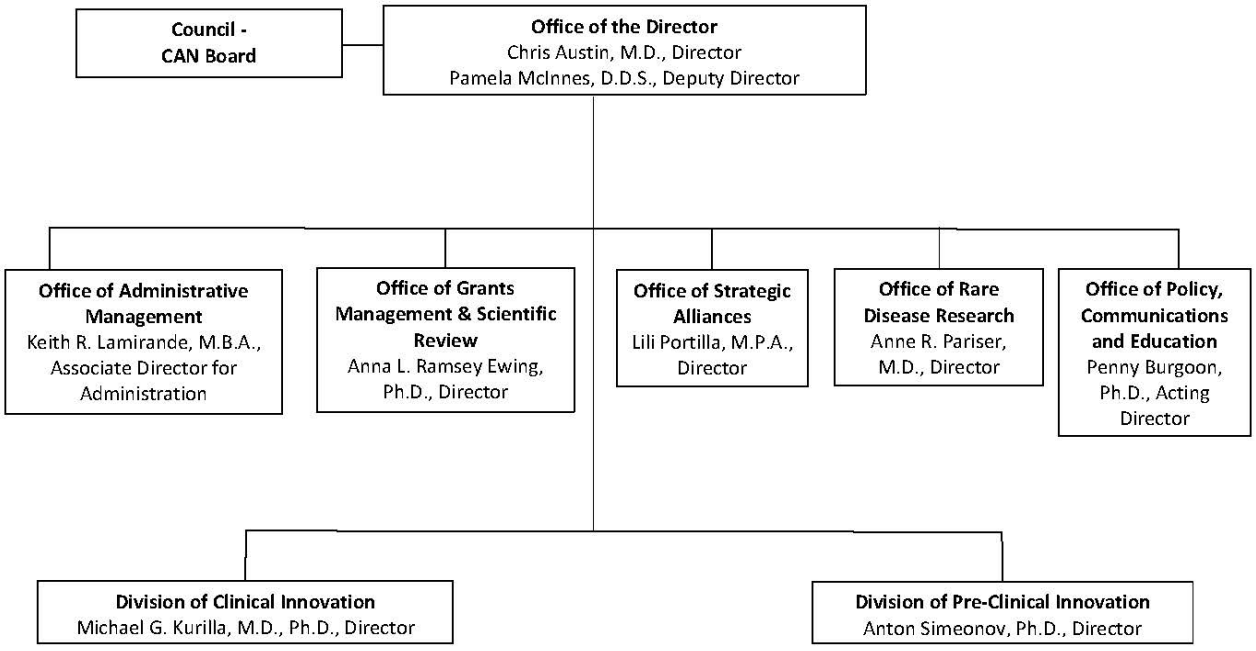
DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

National Center for Advancing Translational Sciences (NCATS)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For carrying out section 301 and title IV of the PHS Act with respect to translational sciences, $685,087,000: Provided, That up to 10 percent of the amount available under this heading shall be available to implement section 480 of the PHS Act, relating to the Cures Acceleration Network

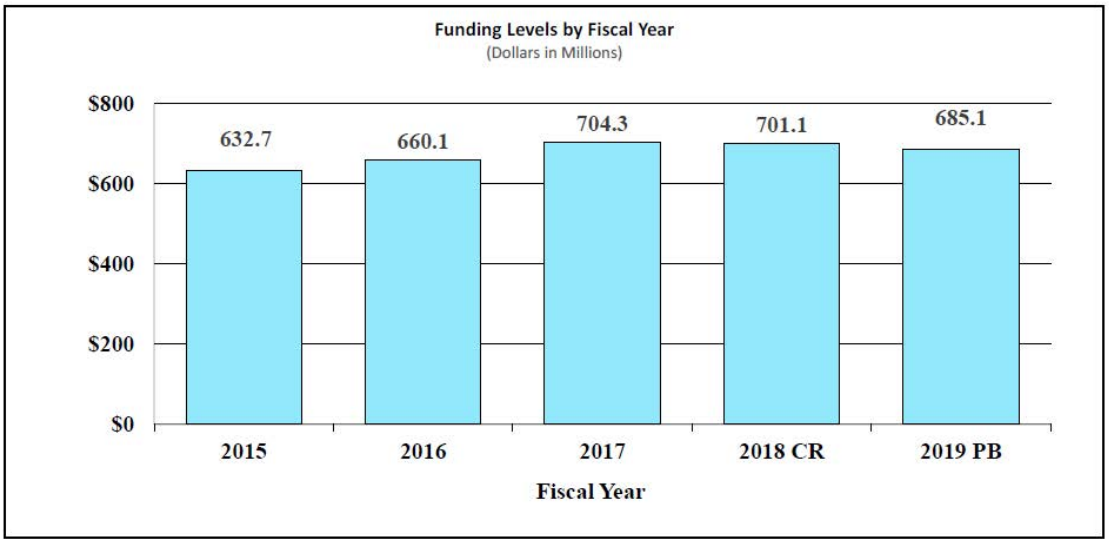
Amounts Available for Obligation[1]

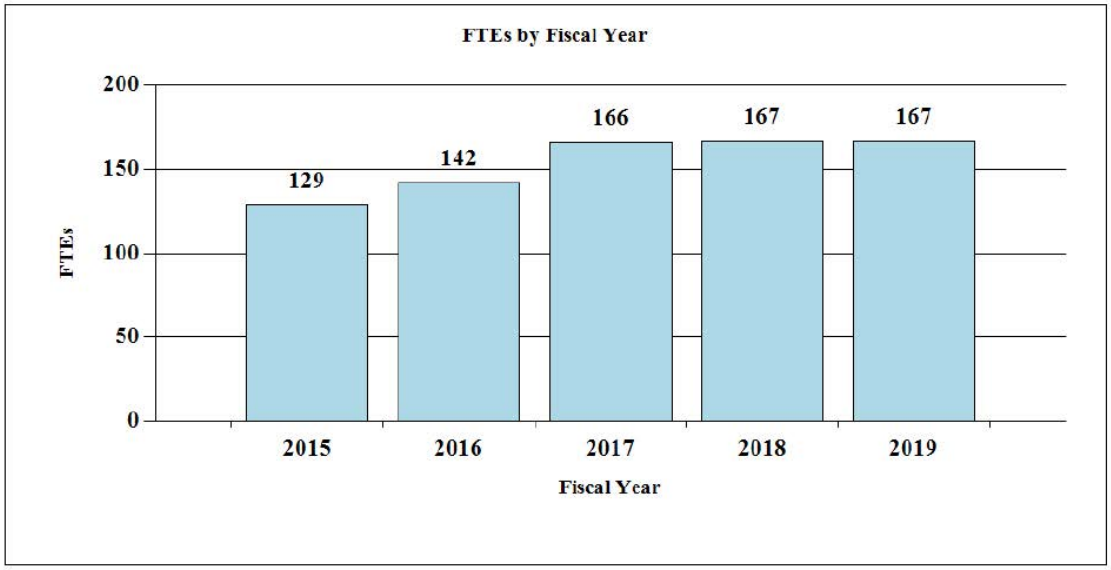
(Dollars in Thousands)

Source of Funding	FY 2017 Final	FY 2018 Annualized CR	FY 2019 President's Budget
Appropriation	$705,903	$705,903	$685,087
Mandatory Appropriation: (non-add)			
Type 1 Diabetes	*(0)*	*(0)*	*(0)*
Other Mandatory financing	*(0)*	*(0)*	*(0)*
Rescission	0	-4,794	0
Sequestration	0	0	0
Secretary's Transfer	-1,573		
Subtotal, adjusted appropriation	$704,330	$701,109	$685,087
OAR HIV/AIDS Transfers	0	0	0
Subtotal, adjusted budget authority	$704,330	$701,109	$685,087
Unobligated balance, start of year	0	0	0
Unobligated balance, end of year	0	0	0
Subtotal, adjusted budget authority	$704,330	$701,109	$685,087
Unobligated balance lapsing	-82	0	0
Total obligations	$704,248	$701,109	$685,087

[1] Excludes the following amounts (in thousand) for reimbursable activities carried out by this account:
FY 2017 - $19,817 FY 2018 - $25,000 FY 2019 - $17,500

History of Budget Authority and FTEs:





Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	2018 Amount Authorized	FY 2018 Annualized CR	2019 Amount Authorized	FY 2019 President's Budget
Research and Investigation	Section 301	42§241	Indefinite	$701,109,213	Indefinite	$685,087,000
National Center for Advancing Translational Sciences	Section 401(a)	42§281	Indefinite		Indefinite	
Total, Budget Authority				$701,109,213		$685,087,000

NATIONAL INSTITUTES OF HEALTH
National Center for Advancing Translational Sciences

Appropriations History

Fiscal Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
2009				
Rescission				$0
2010				
Rescission				$0
2011				
Rescission				$0
2012	$721,601,000		$582,326,000	$576,456,000
Rescission				$1,089,502
2013	$639,033,000		$631,346,000	$575,366,498
Rescission				$1,150,733
Sequestration				($28,879,442)
2014	$665,688,000		$661,264,000	$633,267,000
Rescission				$0
2015	$657,471,000			$635,230,000
Rescission				$0
2016	$660,131,000	$643,111,000	$699,319,000	$685,417,000
Rescission				$0
2017[1]	$685,417,000	$707,335,000	$713,849,000	$705,903,000
Rescission				$0
2018	$557,373,000	$718,867,000	$729,094,000	$705,903,000
Rescission				$4,793,788
2019	$685,087,000			

[1] Budget Estimate to Congress includes mandatory financing.

Justification of Budget Request

Authorizing Legislation: Section 301 and title IV of the Public Health Service Act, as amended, and Section 480 of the PHS Act, relating to the Cures Acceleration Network.

Budget Authority (BA):

	FY 2017 Final	FY 2018 Annualized CR	FY 2019 President's Budget	FY 2019 +/- FY 2018
BA	$704,330,000	$701,109,213	$685,087,000	- $16,022,213
FTEs	166	167	167	-

Program funds are allocated as follows: Competitive Grants/Cooperative Agreements, Contracts, Direct Federal/Intramural, and Other.

Director's Overview

The National Center for Advancing Translational Sciences (NCATS) is dedicated to understanding and innovating on the scientific process by which fundamental discoveries are transformed into interventions that improve human health, in order to get more and better treatments to more patients more quickly. ***Translation*** is the process of turning observations in the laboratory, clinic, and community into interventions that improve the health of individuals and the public, whether those interventions be diagnostics, therapeutics, medical procedures, or behavioral changes.

Our lack of understanding the science of the translational process has enormous human and financial costs: most attempts to develop new interventions fail, preventing new treatments from getting to patients; for example, developing a new drug requires an average 15 years and more than $2 billion given the high prevalence of failure[1]. New treatments may not address the health issues most important to patients. And even after a new intervention is developed, it can take over a decade for the treatment to reach all who could benefit.

NCATS is the first and only organization in the world focused on improving the science of translation. The Center identifies general principles of successful translation and disseminates them for use by the entire biomedical research ecosystem, thus catalyzing more efficient and effective development of new diagnostics and treatments for all diseases. The translational process begins with cell and animal testing (termed "pre-clinical" translation) and continues with studies of diseases tests of therapies in people (collectively referred to as "clinical" translation). NCATS innovates in all of these areas[2].

[1] Pharmaceutical Research and Manufacturers of America. 2016 biopharmaceutical research industry profile. Washington, DC: PhRMA; April 2016.
[2] https://ncats.nih.gov/translation/spectrum

In the pre-clinical translation, NCATS is focused on the four predominant causes of failure:

"Target validation," where a particular disease-related molecular malfunction is chosen for therapeutic development. Target validation often fails due to limitations in chemistry. Known chemical structures are able to affect only 10 percent of potential drug targets, greatly limiting new drug development for currently untreatable diseases. NCATS is therefore launching an ambitious multi-disciplinary initiative to bring together and innovate chemistry, robotic engineering, biological activity testing, and machine learning/artificial intelligence to transform the exploration of novel chemical space for new drug discovery. Through its **Automated Synthesis Platform for Innovative Research and Execution** (ASPIRE) initiative, the Center will develop a research platform in which novel chemical compounds are rapidly synthesized and tested for their potential to influence disease processes. Such a system could significantly expand the known universe of drugs with the potential to improve human health.

"Efficacy testing," in which an intervention is tested for a desired effect in cell or animal models. Efficacy testing is frequently misleading due to the rudimentary nature of the testing systems used to identify new drugs. To address this problem, NCATS has started an ambitious **3D Bioprinting** program of human tissues to enable massive parallel testing of new drugs. This bioprinting initiative, supported through NCATS' Cures Acceleration Network (CAN), is currently printing miniature skin, retina, and blood vessel tissues that promise to mimic human function and disease, and thus provide a much more accurate way to identify new drugs.

"Toxicity testing," where drugs are assessed for their safety prior to human testing. This process utilizes multiple species of animals and frequently does not predict adverse effects of drugs in humans. NCATS' **Tissue Chip for Drug Screening** program has created microfluidic engineered systems made with human cells that represent all major human organs, and is working closely with the FDA and pharmaceutical companies to validate their use in drug development. NCATS' efforts have stimulated interest in this now-rapidly developing field, which promises to make toxicity testing more rapid and accurate. Translation is a bidirectional process, and the Tissue Chip program has a new effort to model human diseases in these tissue chip microfluidic platforms. NCATS is collaborating with many other NIH Institutes and Centers to support the development of more than a dozen "organs on chips" to advance our understanding of these diseases as well as provide platforms for testing of new drugs for them.

"De-risking" is a process in which an intervention is fully developed and approved for clinical testing by the FDA. De-risking is the focus of the NCATS **Therapeutics for Rare and Neglected Diseases** (TRND) program, which works closely with academic, biopharmaceutical, foundation, and regulatory partners to develop and test new technologies and paradigms to increase the efficiency and effectiveness of intervention development for human testing. For example, NCATS is developing platform technologies to catalyze application of gene therapy to many rare diseases simultaneously. Working with Agilis Biotherapeutics, a startup biotechnology company in Boston, NCATS is developing and testing this technology in a devastating and currently untreatable disease of children, Aromatic Amino Acid Decarboxylase Deficiency.

Teamwork and collaboration is central tenet of NCATS. Success translation requires a team approach; it could not be accomplished by a single individual or even organization. NCATS considers the FDA as a key partner in translation. NCATS and the FDA's Office of Orphan Products Development are jointly funding natural history studies for rare diseases. This effort will provide information on the progression of rare diseases, lack of which is a major cause of rare disease drug development failure. These studies and the broad natural history registry program[3] that NCATS is developing through its Office of Rare Diseases Research will generate new knowledge for the development of new treatments for rare diseases.

In the clinical domain, NCATS' flagship **Clinical and Translational Science Awards** (CTSA) Program comprises a suite of initiatives focused on understanding and reversing the causes of clinical translational failure, which prevent new interventions from being successfully tested in and made available to patients. For example, a single institutional review board (IRB) platform to conduct a study's ethics review for multisite clinical studies has been developed by program grantees: the NCATS **Streamlined, Multisite, Accelerated Resources for Trials (SMART) IRB** Platform. SMART IRB will shorten the time of review as one site assumes the IRB responsibilities for all study sites, one of the most long-standing and previously intractable problems in getting clinical studies started.

The CTSA Program Accrual to Clinical Trials (ACT) is developing a platform that uses electronic health records to identify patients who might be eligible for clinical studies. In addition, NCATS CTSA Program grantees have created a more patient/doctor friendly portal for ClinicalTrials.gov information called *Trials Today*, and a major effort to increase minority clinical study recruitment called *Faster Together*. Together, these initiatives will facilitate both clinical researchers' identification of potential participants, and patients' identification of clinical research studies in which they may want to participate.

Training and workforce development are a major NCATS priority because translation requires knowledge, skills, and attitudes distinct from other areas of science. An exciting training innovation in the CTSA Program is the advent of "externships" in which trainees spend extended time in another part of the translational ecosystem, such as a biopharma company, regulatory agency, or patient advocacy organization. These externships are enormously beneficial to the training of truly "multilingual" translational scientists. An analogous effort among the CTSA Program institutions now enables trainees to obtain part of their training at a different CTSA Program hub, taking advantage of the enormous diversity of different translational strengths network. In another of NCATS' clinical programs, the Rare Diseases Clinical Research Network (RDCRN), trainees learn the team science so essential to translation by intensive project team work with academic, patient advocate, and pharmaceutical partners. Training has also gone global, with the NCATS online Assay Guidance Manual for preclinical translation being viewed by over 40,000 users every month in every state in the U.S. and over 100 countries. These innovative programs are providing opportunities, never before possible, and are producing translational scientists with new insights into the translational process and the capacity to drive the translational science agenda in the coming decades.

[3] https://ncats.nih.gov/radar

Including patients as members of the research team is an NCATS priority that promises to make translational research projects more efficient, effective, and relevant. Like other areas of translational science, however, best practices and measurement outcomes require development. NCATS is teaming with patients and scientists to develop the science of patient input. A major step forward is the co-development by NCATS and patient groups of the NCATS Toolkit for Patient-Focused Therapy Development, an online portal[4]. This compilation of "how-to" resources – many developed by patient groups – spans the therapeutic development landscape from discovery through clinical trials, to regulatory review and post-marketing studies; and will empower patients to learn about and become involved in translational research. While developed with a rare disease focus, the tools provided in the Toolkit are applicable to all diseases.

The field of translational science is young and much remains to be accomplished, but the pace of progress portends a bright future for translation, its practitioners, and most importantly, for the patients who will be its beneficiaries.

Program Descriptions and Accomplishments

Clinical and Translational Science Activities

NCATS has evolved the CTSA Program into a multifaceted scientific program that nurtures the particular translational strengths of individual institutions (called "hubs"). Cross-hub collaborations are enabled through the program for joint development of solutions to systemic translational challenges such as sharing of information, and creating flexibility and capacity to bring together biomedical research institutions to address system-wide issues in clinical research and translational science.

The process of obtaining ethical approval for a multisite clinical trial by multiple institutional review boards (IRBs) is a longstanding challenge to clinical research. Obtaining ethics review approval across several IRBs leads to significant delays in study activation and can result in inconsistent review of study conduct across sites. One way to provide more consistent, high-quality IRB review is by having all participating sites in a study rely on a single IRB. CTSA Program investigators established the NCATS SMART IRB Platform. This resource aligns with NIH's single IRB policy for multisite clinical research that was announced June 21, 2016. As of March 23, 2017, all CTSA Program hubs had signed on to the SMART IRB authorization agreement. By the fall of 2017, approximately 300 research institutions across the nation were participating in SMART IRB, making it possible to initiate a multisite clinical study within weeks instead of months.

The most recent funding opportunity announcement (FOA) to solicit applications for CTSA Program hub awards expired in FY 2018. NCATS sought input from stakeholders, including hub principal investigators and Congress, prior to issuance of a new FOA in FY 2019.

- **CTSA Program Collaborative Innovation Awards (CCIA):** CCIA projects support research collaborations across three or more CTSA Program hubs to develop, demonstrate, and disseminate innovative, experimental approaches to overcoming systemic translational

[4] https://ncats.nih.gov/toolkit

science roadblocks. One such exciting project is Strengthening Translational Research in Diverse Enrollment (STRIDE), through which NCATS grantees are developing, testing, and disseminating an integrated multi-level, culturally sensitive intervention to engage African Americans and Latinos in translational research. STRIDE is a partnership among the CTSA Program hubs in three geographically diverse areas with large African American and Latino populations: University of Massachusetts Medical School, University of Alabama at Birmingham, and Vanderbilt University.

- **NCATS Trial Innovation Network**: The Trial Innovation Network is a collaboration among distinguished clinical researchers from multiple CTSA Program hubs which is composed of three key organizational partners: the Trial Innovation Centers, the Recruitment Innovation Center, and the CTSA Program hubs. Innovative solutions for addressing critical roadblocks in the conduct of, and operations for, clinical research will be pilot tested for potential availability across the CTSA Program. The network is not meant as permanent infrastructure for running clinical trials, but rather is focused on clinical trial operational innovation and collaboration for enhancing the efficiency and effectiveness of how clinical research is conducted. Network investigators will use and pilot test the NCATS SMART IRB Platform, master contracting agreements, and quality-by-design approaches, and also focus on evidence-based strategies for study recruitment and patient engagement.

- **CTSA Program Data to Health (CD2H) Program**: Initially funded in FY 2017, CD2H investigators will work with all CTSA Program-supported institutions to: 1) support and enhance a collaborative informatics community for the CTSA Program; 2) develop Good Data Practices for information stewardship; 3) promote software standards for interoperability; 4) foster collaborative innovation in the area of informatics tools, methods, and processes; 5) stimulate the use of cutting-edge biomedical research informatics and data science education for CTSA Program researchers; and 6) evaluate the impact of CD2H activities to enhance health through the use of informatics resources. Through these activities, the CD2H will support CTSA Program-supported institutions with solutions to and innovations in health information management that will facilitate data sharing across the CTSA Program network and ultimately other institutions engaged in clinical research.

- **Common Metrics Initiative**: A key recommendation of the 2013 Institute of Medicine (now the National Academy of Medicine) report on the CTSA Program was to develop objective and measurable outcome measures for the productivity and impact of the CTSA Program hubs and the program as a whole. NCATS and the CTSA Program investigators share this vision and have approached the development of such measures as a translational science problem. NCATS and the CTSA Program hub investigators have developed an experimental approach called the Common Metrics Initiative, which is intended to provide measurable indicators of the program's success. Three common metrics have so far been developed and implemented: IRB duration, sustainability of scholars in translational science research careers, and publications resulting from CTSA Program-provided pilot funding. Two additional metrics are under development for clinical research participant accrual and data warehouse interoperability.

- **CTSA Program Data Coordinating Center:** In FY 2017, NCATS issued a new award for the CTSA Program Data Coordinating Center to the Center for Leading Innovation and Collaboration (CLIC), at the University of Rochester. The CLIC is developing virtual and in-person platforms through which CTSA Program institutions can share data and educational materials, track their success, communicate with one another, and develop collaborations. These efforts will help CTSA Program-funded institutions benchmark their progress in comparison to the network as a whole and identify areas where improvement may be needed.

- **CTSA Program Training and Career Development:** Providing the resources to train, cultivate, and sustain future leaders of the biomedical research workforce is a key CTSA Program goal. Program support enables a coordinated, national effort to help ensure that our nation will have a pipeline of trained investigators who can move basic research findings into applications for improving health as novel therapies, diagnostics, and preventives. Scientists and clinicians gain practical research experience by working with interdisciplinary teams guided by experienced mentors. This team-science approach helps prepare clinician-scientists to better address today's complex research challenges.

  The CTSA Program supports two types of formal clinical research training. Both programs combine formal course work with direct research experience, and many institutions' programs offer opportunities to pursue additional advanced degrees. All CTSA Program hubs have a career development program which offers formal research training experience to scholars who already have an M.D., Ph.D., or equivalent doctoral degree. Many CTSA Program hubs also receive predoctoral trainee awards to support a program for an introduction to clinical and translational.

Program Portrait: CTSA Program Training to Drive Discovery to Commercialization for Brain Tumors

Through the University of North Carolina Translational and Clinical Sciences Institute, a mentored clinical research scholar received the translational science training needed to support his research and to springboard his career to academic independence. The scholar worked with mentors to develop a potential therapy for converting a patient's skin cells into a personalized, tumor-targeting stem cell treatment against glioblastoma multiforme, an aggressive brain cancer. In the clinical setting, the final product would be the first of its kind to enable efficient delivery of an anti-cancer agent into the tumor cavity of brain cancer patients. At the delivery site, the therapeutic stem cells would seek out residual tumor cells that cannot be treated through standard surgery and chemotherapy. The university's career development program supported the scholar with training in important translational science career skills, from how to manage a lab and write grants, to understanding the drug development process and therapeutic product development. The scholar engaged with patient and clinical stakeholders and business experts, resulting in an award from the Eshelman Institute for Innovation, a grant from the state of North Carolina, and a newly funded investigator-initiated research project grant from NIH. In addition, he has filed two provisional patent applications and launched a new company based on stem cell technology.

CTSA Program grantees have developed a set of national training resources for clinical and translational sciences, including educational core competencies, best practices for training mentors, and curriculum materials for training courses. These educational resources are freely available, and many institutions have integrated them into their training programs.

- **CTSA Program I-Corps "Train-the-Trainer" Initiative:** NCATS is among 17 NIH ICs to participate in the NIH Innovation Corps (NIH I-Corps) Program. The NIH I-Corps program is a collaborative effort with the National Science Foundation to support the development and commercialization of biomedical technologies. The NCATS CTSA Program also features an I-Corps "Train-the-Trainer" initiative that not only teaches investigators how to move research discoveries and technologies toward commercialization, but also has them train additional trainees to cultivate a cadre of business-savvy researchers.

- **NCATS-Eli Lilly Scholars Externship Program:** In translational science, the space between academic and industry research is often referred to as the great divide. Not only are there different laboratory environments and cultures, historically, there has not been much opportunity for researchers in these separate sectors to interact with each other. To help scientists bridge the gap, NCATS is partnering with Eli Lilly and Company on the NCATS-Eli Lilly scholars externship program. Similar to a study-abroad program, the externship pairs scholars, trainees, and investigators from the CTSA Program with an Eli Lilly project team for up to one year at Eli Lilly's headquarters in Indianapolis. The externship is a fully immersive experience that enhances collaboration between academic researchers and industry scientists, exposing the trainees to the techniques and strategies of industry research.

Rare Diseases Research and Therapeutics

In the U. S., a rare disease is defined as a disease or condition that affects fewer than 200,000 individuals.[5] There are about 7,000 rare diseases affecting an estimated 25 million Americans.[6] Most of these diseases are serious or life-threatening, progressive, chronic illnesses that result in disability and often lead to premature death; most (approximately 80 percent) are genetic, and many affect infants and children. Though research progress has been made, few drug companies develop treatments for rare diseases, and more than 95 percent of rare diseases have no approved treatment.[7] NCATS supports several translational science programs and activities to address the translational research needs of rare diseases patients and to accelerate the rare diseases research process intended to deliver treatments to these patients faster.

- **Therapeutics for Rare and Neglected Diseases (TRND)**: Through its TRND program, NCATS supports pre-clinical development of therapeutic candidates intended to treat rare or neglected disorders, with the goal of submitting a successful Investigational New Drug (IND) application to the FDA. NCATS provides therapeutic development expertise and resources to collaborate with research partners and content experts — such as NIH's Institutes and Centers (ICs), academic scientists, nonprofit organizations, and pharmaceutical and biotechnology companies working on rare and neglected illnesses — to move therapeutics through pre-clinical testing, including plan development for clinical trials and submission of an IND application. When successful, these efforts effectively "de-risk" therapeutic candidates, making them more attractive for adoption by outside business partners for continued development.

[5] Orphan Drug Act of 1983 (P.L. 97-414), as amended
[6] Rare Diseases Act of 2002 (P.L. 107-280), as amended
[7] FDA Office of Orphan Products Development

Program Portrait: Gene Therapy for AADC Deficiency

Through the TRND program, NCATS has expanded its project portfolio to include gene therapy pre-clinical development. A collaboration between NCATS' TRND researchers and Agilis Biotherapeutics, Inc., of Cambridge, Massachusetts, has resulted in a gene therapy moving closer to market years ahead of schedule. Following a recent meeting with the FDA, Agilis will begin the process of seeking final approval to treat U.S. patients with the rare pediatric condition aromatic L-amino acid decarboxylase (AADC) deficiency, which is a life-threatening disorder. The AADC enzyme is necessary to produce important chemical messengers in the brain and other parts of the central nervous system. Children with AADC deficiency commonly experience severe developmental delays, weak muscle tone, and involuntary movement of the limbs. There is no approved treatment for AADC deficiency, and patients with severe forms of the disorder usually die in the first decade of life. The gene therapy, called AGIL-AADC, restores AADC enzyme production in the brain. Agilis licensed the gene therapy from National Taiwan University, where investigators had conducted clinical studies on patients with severe AADC deficiency. While those studies showed sustained improvements following a single dose of AGIL-AADC, the investigators lacked pre-clinical data required by the FDA. The small market for this ultra-rare disease and the need to conduct additional studies threatened to stall the project. Agilis partnered with NCATS' TRND scientists to further develop AGIL-AADC in several ways, including conducting pre-clinical safety studies and producing AGIL-AADC in a way that met FDA requirements. In just over a year, these efforts led to a meeting with the FDA to review the pre-clinical, clinical, and manufacturing data. In an unusual step, FDA reviewers determined that Agilis did not have to repeat clinical trials in the United States, clearing the path for the company to file a Biologics Licensing Application which, if approved, would allow the company to market AGIL-AADC to patients. AGIL-AADC is poised to be among the first FDA-approved gene therapies for treating a central nervous system disorder. Moreover, it would be the first therapy supported by NCATS, through its TRND program, to receive marketing approval from the FDA and become available to patients.

- **Rare Diseases Clinical Research Network (RDCRN):** Through its RDCRN program, NCATS provides support for collaborative, rare diseases-focused research networks that include clinical studies, diagnosis, patient involvement, study enrollment, translational research, data sharing, and training for young investigators. The program features 21 clinical research consortia and a data management and coordination center, all of which are overseen by NCATS with scientific participation and additional support from nine NIH ICs. Additionally, patient organizations may contribute funding to support the consortium. Each RDCRN consortia must focus on at least three related rare diseases and involve a patient advocacy group in the research with the expectation that resources, experts, and knowledge can be shared for greater impact. As a result, scientists supported by the RDCRN study more than 220 rare diseases. The consortium also provides unique translational training required for scientists who study rare diseases. In FY 2018, NCATS issued a new FOA for applications to the RDCRN.

- **Genetic and Rare Diseases Information Center (GARD):** An important part of NCATS mission is to make accessible, up-to-date research information on genetic and rare diseases easily available to the public. NCATS collaborates with NHGRI to support the Genetic and Rare Diseases Information Center. Through GARD, NCATS and NHGRI provide comprehensive, and easy-to-understand information about rare and genetic diseases to patients, their families, health care providers, researchers, and the public. GARD information specialists are available to discuss questions by phone and email in English and Spanish. Upon request, GARD volunteers also can provide translations of information into other languages, including French, Portuguese, Russian, and German. In 2017, more than 5 million people visited the GARD webpages.

Program Portrait: NCATS Toolkit for Patient-Focused Therapy Development

NCATS is dedicated to engaging the patient community throughout the translational science process and to helping them to become a part of the biomedical research team. In the fall of 2017, the Center launched its Toolkit for Patient-Focused Therapy Development (Toolkit) to provide a collection of online resources that can help patients and their support organizations understand and participate in research and therapy development. The Toolkit includes resources developed by patients and for patients, and while the tools have been developed primarily for the rare diseases community, many of them can be used by people suffering from any disease or disorder. To create the Toolkit, NCATS worked with a diverse group of partners in the rare diseases community to conduct an extensive landscape analysis of available tools. These resources were defined, characterized, and organized in the centralized Toolkit portal that can be helpful to all patient support groups with all levels of knowledge about translational science. NCATS will continue to work with patient groups to improve this resource and support its dissemination.

- **Natural History Studies for Rare Diseases:** Evaluating a new treatment against the background of the disease itself is based on so called "natural history," datasets that come from patient, family, and clinician observations of a given condition over time. NCATS has supported natural history studies through its RDCRN and has partnered with the FDA Office of Orphan Products Development to award grants in FY 2017. Through such research, NCATS gains access to natural history data, which can subsequently guide the design of subsequent clinical trials.

Re-Engineering Translational Sciences

NCATS applies innovation to scientific and operational bottlenecks that stop translational research progress. By applying resources, expertise, and ingenuity in a targeted manner, NCATS initiatives bridge or reignite science discovery, and return research momentum to a project, even after Center contributions are complete.

- **Discovering New Therapeutic Uses for Existing Molecules (New Therapeutic Uses):** NCATS' New Therapeutic Uses program aims to improve the process of developing new treatments and cures for disease by finding new uses for existing therapies that already have cleared several key steps along the development path. NCATS designed this program to align with one of the Center's primary goals of fostering approaches that improve the translational research efficiency and ultimately accelerate the pace at which discoveries are turned into new preventions, treatments, and cures for human diseases.

    - **NIH-Industry Partnerships Initiative:** NCATS continues to foster collaboration between pharmaceutical companies and the biomedical research community to advance therapeutics development. The focus is on matching researchers to a selection of pharmaceutical assets to help the scientists test ideas for a new therapeutic use or indication. The New Therapeutic Uses program provides model template agreements between NIH and the pharmaceutical company, and between the company and the biomedical research partner. These template agreements reduce the time required to establish collaborations between industry and academia to as few as three months from the more typical nine months to one year.

    - **Bench-to-Clinic Repurposing Initiative:** Through this new initiative, NCATS supports drug repurposing pre-clinical studies where investigators must apply innovative processes

for identifying the therapeutic/indication pair, such as the use of crowdsourcing strategies, computational algorithms, or big datasets from patient records to predict new uses of a drug or biologic. These pre-clinical studies will present an opportunity to demonstrate the usefulness of a drug-indication pairing method. If proven successful, the therapeutic/indication pairing strategy can be adopted by the broader scientific community to improve the process of predicting new indications for existing therapeutics.

- **Assay Guidance Manual (AGM):** The Assay Guidance Manual is a best-practices online resource that is accessible from both the NCATS and the National Library of Medicine websites. The AGM supports translational science by sharing up-to-date information devoted to the successful development of robust, early-stage drug discovery assays. NCATS manages and regularly updates the content of the manual with input from industry, academia, and government experts. NCATS also provides training workshops on how to use the AGM, including the sharing of best practices and advice on robust assay design, development, and implementation. NCATS' training seminars on the use of the AGM has raised awareness about this valuable resource. In 2016, the AGM was accessed 375,000 times — more than 1,000 "hits" a day.

- **NCATS Chemical Genomics Center (NCGC):** NCATS researchers collaborate with investigators in the NIH, academia, biopharmaceutical, and nonprofit sectors to generate probes for studying a diverse cross-section of human biology, focusing specifically on new targets for diseases with no treatments. Through the NCGC, NCATS also supports research in probe development which includes the use of small molecules that can be used as chemical probes to study the functions of genes, cells, and biochemical pathways.

  NCATS' NCGC and University of Nevada, Reno School of Medicine researchers together demonstrated that a drug originally designed to treat cancer may have new life as a potential treatment for Duchenne muscular dystrophy (DMD). This collaborative team screened more than 350,000 compounds to find SU9516, which had been previously developed as a treatment for leukemia. The research demonstrated that this compound improved muscle function in both laboratory and animal DMD models. The results may provide a promising approach against the disorder and other muscle-wasting conditions.

Cures Acceleration Network (CAN)

Congress created the Cures Acceleration Network (CAN) to advance the development of high-need cures and to reduce significant barriers between research discovery and clinical trials. To achieve these objectives, the Public Health Service Act authorizes CAN to make large grant awards of up to $15 million per fiscal year, partnership awards that require 1:3 matching funds, and flexible research awards using the special authorization called other transaction authority (OTA), when grants, contracts, and cooperative agreements may not adequately address scientific needs. NCATS staff uses the OTA mechanism to attract non-traditional government partners, and to expand, modify, and, if needed, discontinue activities to meet program needs. CAN investments are guided by the NCATS CAN Review Board.

Based on available funds each fiscal year, through CAN, NCATS invests in high-risk, high reward initiatives designed to address significant scientific and technical challenges that hinder

translational research. CAN currently supports NCATS' Tissue Chip for Drug Screening, Biomedical Data Translator, and Three-Dimensional Bioprinting programs, as well as the new Automated Synthesis Platform for Innovative Research and Execution (ASPIRE) initiative.

- **Tissue Chip for Drug Screening (Tissue Chip):** As an effort originally designed to revolutionize the process for predicting drug safety, NCATS' Tissue Chip program began with researchers developing miniaturized platforms that could support miniature models of living organs — such as the lung, liver, and heart — that could be integrated into connected organ systems. Initially, Tissue Chip was an NIH Common Fund program in collaboration with other NIH ICs, the Defense Advanced Research Projects Agency, and the FDA. The program is now funded and administered through NCATS and has been expanded in new scientific directions to advance translational research and the science of translation itself. New Tissue Chip initiatives were funded in FY 2017 and this support will continue into FY 2019.

    - **Tissue Chip Testing Centers:** Center investigators independently test and validate tissue chips to determine if they perform as designed. These scientists establish and apply standardized methods for tissue chip pre-clinical testing of any drug or biologic to ensure and wide-ranging availability of tissue chip technology, particularly for regulatory agencies and pharmaceutical companies, and help promote the adoption of this technology by the larger research community.

    - **Tissue Chips for Disease Modeling and Efficacy Testing:** NCATS supports the scientific expansion of the Tissue Chip program to support development of tissue chip models of human disease. Thirteen awards in FY 2017 are supporting tissue chips designed to model brain, lungs, heart, joints, and kidney diseases. Recognizing the value of this initiative to their missions, other NIH ICs, and Offices are participating partners. This funding opportunity will be extended to FY 2018, enabling NCATS and its NIH collaborators to fund additional chips.

    - **Tissue Chips in Space:** NCATS and the Center for the Advancement of Science in Space (CASIS) partnered to refine tissue chip technology for translational research at the International Space Station U.S. National Laboratory (ISS-NL). It is widely known that symptoms of accelerated aging — such as muscle deterioration, osteoporosis (bone loss) — occur after prolonged exposure to microgravity. Tissue chip translational science at the ISS-NL could reveal molecular targets that can slow that process. NCATS issued five awards in FY 2017 to develop these models to facilitate the assessment of biomarkers, bioavailability, efficacy, and toxicity of therapeutic agents for testing at the ISS-NL. The launch date for sending the chips to the ISS-NL is anticipated for December 2018. Data from this research will help scientists develop and advance novel technologies to improve human health here on Earth.

- **Biomedical Data Translator (Translator):** Through its Translator program, NCATS is integrating patient and biomedical data to facilitate connections between these disparate types of information, with the potential for generating new knowledge and strategies for research and treatment. If successful, Translator will be a tool capable of linking these

existing sources of data in new ways and may create new research and treatment inroads to multiple diseases and disorders.

In September 2017, NCATS announced a novel application process that included successful completion of a series of computational tasks, called the "Challenge," as the first part of a three-step application process to move to the next step of accessing the complete funding opportunity announcement to submit a concept letter. Challenge tasks were designed not only to provide applicants with important background and insights for building a reasoning tool prototype that would be interoperable with existing components of the Translator, but also to demonstrate whether applicants have the necessary skills to quickly integrate with and contribute to Translator efforts already in progress. Teams receiving positive reviews of their concept letters will move to the final steps of submitting a full proposal and participating in a virtual meeting with the review panel in late FY 2017. This unique application process was made possible through the CAN OTA.

- **Three-Dimensional Bioprinting (3-D Bioprinting):** NCATS established the 3-D Bioprinting laboratory to generate live, human tissues that can be reliably reproduced for drug screening, where automation is leveraged to quickly test the biochemical activity of a large number of compounds. This ability to reproduce, repeatedly and rapidly, models of human tissues that faithfully characterize native human tissue is expected to generate clinically-relevant data to make the drug discovery process more predictable and efficient.

  NCATS has developed a printed skin tissue model virtually equivalent to real human skin when comparing histological cross-sections, and, in collaboration with the National Eye Institute, an ocular tissue model which displays proper structure and function of the outer blood retina barrier in the back of the eye. It amazingly mimics pathological conditions of age-related macular degeneration — the leading cause of vision loss, affecting more than 10 million Americans — more than cataracts and glaucoma combined. These and other 3-D tissue models are being developed, optimized, and validated.

- **Automated Synthesis Platform for Innovative Research and Execution (ASPIRE)**: The scientific field of medicinal chemistry, including early phase drug discovery and chemical synthesis have changed little over the past century. The processes for early pharmaceutical development remain largely labor-intensive and non-mechanized. Through ASPIRE, NCATS will apply innovation and automation to transform medicinal chemistry from an individualized craft to a modern, information-based science — an effort that ultimately will result in more rapid testing and development of potential chemical compounds as treatments for diseases and other conditions. Automated chemistry synthesis applied to drug design will address long-standing challenges, including lack of standardization, low reproducibility, and an inability to predict how new chemicals will behave. The tools developed through ASPIRE initiative will minimize the amount of time chemists spend on tedious and repetitive tasks, freeing them up for more complicated pursuits such as designing compounds for diseases that have no medical treatment. In addition, ASPIRE has the potential to help biomedical scientists whose primary expertise is not in chemistry to effectively translate their cellular and molecular ideas into testable chemical compounds.

Translational Research Resources (TRR)
NCATS' TRR funds scientific conference grants, often in collaboration with other NIH ICs, and trans-NIH supported research programs and initiatives. The support includes rare disease research conferences, which are an important vehicle for advancing related research because they provide an environment for discussion about the state of the science. These conferences also facilitate research collaborations and bring together the broader research community, including researchers, clinicians, patient groups, and other allied health professionals to share novel advances and develop best practices and guidelines.

Intramural Research Program (IRP)
NCATS' Division of Pre-Clinical Innovation (DPI) plans, conducts, and advances research in a highly and uniquely collaborative manner across the pre-clinical phases of the translational science spectrum. Its expertise and state-of-the-art laboratories have been invaluable in advancing breakthrough technology and transforming translational science. NCATS matches these expertise and technology resources with NIH-supported extramural investigators, other NIH IC IRP investigators, and additional collaborators necessary to advance the scientific goals of a project. NCATS contributes state-of-the-art technological resources and operational expertise in pre-clinical therapeutics development, including access to unique pharmacological compounds and tools, establishment of partnership agreements, regulatory support, and access to contract services. As a result, successful collaborations through these programs benefit from Center efforts to improve diagnostics and therapeutics development, and to make translational science more efficient, less expensive, and less risky.

NCATS' DPI programs and accomplishments have been highlighted throughout this budget document. For example, the TRND program has been covered within the Rare Disease Research activity description (page 15), and 3-D Bioprinting and ASPIRE are described within the Cures Acceleration Network section (page 17).

Research Management and Support (RMS)
The RMS budget supports the scientific, administrative management, communications, and information technology activities associated with NCATS' operations. These activities support collaborative interactions with NCATS' grantees, and the review, award, and monitoring of research grants, training awards, and research and development contracts.

Detail of Full-Time Equivalent Employment (FTE)

OFFICE/DIVISION	FY 2017 Final			FY 2018 Annualized CR			FY 2019 President's Budget		
	Civilian	Military	Total	Civilian	Military	Total	Civilian	Military	Total
Division of Clinical Innovation									
Direct:	20	1	21	21	1	22	21	1	22
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	20	1	21	21	1	22	21	1	22
Division of Pre-Clinical Innovation									
Direct:	40	-	40	40	-	40	40	-	40
Reimbursable:	5	-	5	5	-	5	5	-	5
Total:	45	-	45	45	-	45	45	-	45
Office of Administrative Management									
Direct:	32	-	32	32	-	32	32	-	32
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	32	-	32	32	-	32	32	-	32
Office of Grants Management and Scientific Review									
Direct:	20	-	20	20	-	20	20	-	20
Reimbursable:	9	-	9	9	-	9	9	-	9
Total:	29	-	29	29	-	29	29	-	29
Office of Policy, Communications, and Education									
Direct:	11	-	11	11	-	11	11	-	11
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	11	-	11	11	-	11	11	-	11
Office of Rare Diseases Research									
Direct:	6	-	6	6	-	6	6	-	6
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	6	-	6	6	-	6	6	-	6
Office of Strategic Alliances									
Direct:	6	-	6	6	-	6	6	-	6
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	6	-	6	6	-	6	6	-	6
Office of the Director									
Direct:	15	-	15	15	-	15	15	-	15
Reimbursable:	1	-	1	1	-	1	1	-	1
Total:	16	-	16	16	-	16	16	-	16
Total	165	1	166	166	1	167	166	1	167
Includes FTEs whose payroll obligations are supported by the NIH Common Fund.									
FTEs supported by funds from Cooperative Research and Development Agreements.	0	0	0	0	0	0	0	0	0

FISCAL YEAR	Average GS Grade
2015	12.8
2016	12.8
2017	12.6
2018	12.6
2019	12.6

Detail of Positions[1]

GRADE	FY 2017 Final	FY 2018 Annualized CR	FY 2019 President's Budget
Total, ES Positions	1	1	1
Total, ES Salary	181,846	185,301	186,181
GM/GS-15	17	17	17
GM/GS-14	26	26	26
GM/GS-13	48	48	48
GS-12	8	9	9
GS-11	7	8	8
GS-10	1	1	1
GS-9	12	11	11
GS-8	4	4	4
GS-7	2	2	2
GS-6	1	1	1
GS-5	0	0	0
GS-4	0	0	0
GS-3	0	0	0
GS-2	0	0	0
GS-1	0	0	0
Subtotal	126	127	127
Grades established by Act of July 1, 1944 (42 U.S.C. 207)	0	0	0
Assistant Surgeon General	0	0	0
Director Grade	1	1	1
Senior Grade	0	0	0
Full Grade	0	0	0
Senior Assistant Grade	0	0	0
Assistant Grade	0	0	0
Subtotal	1	1	1
Ungraded	38	38	38
Total permanent positions	128	129	129
Total positions, end of year	170	175	175
Total full-time equivalent (FTE) employment, end of year	166	167	167
Average ES salary	181,846	185,301	186,181
Average GM/GS grade	12.6	12.6	12.6
Average GM/GS salary	113,838	116,000	116,551

[1] Includes FTEs whose payroll obligations are supported by the NIH Common Fund.