

**Department of Health and Human Services  
National Institutes of Health  
National Center for Advancing Translational Sciences**

**25th Meeting of the  
Advisory Council**

**Minutes of Virtual Meeting  
September 17–18, 2020**

The National Center for Advancing Translational Sciences (NCATS) Advisory Council held a meeting in open session on September 17, 2020, from 1:00 p.m. to 3:00 p.m. and on September 18, 2020, from 11:00 a.m. to 3:00 p.m. ET via Webex. Christopher P. Austin, M.D., NCATS Advisory Council chair, led the meeting. In accordance with Public Law 92-463, the session was open to the public.

Prior to the meeting, the NCATS Advisory Council met in closed session on September 17, 2020, from 11:00 a.m. to 11:56 a.m. for the review and consideration of grant applications.

**NCATS ADVISORY COUNCIL MEMBERS PRESENT**

**Chair**

Christopher P. Austin, M.D., Director, NCATS

**Executive Secretary**

Anna L. Ramsey-Ewing, Ph.D., Director, Office of Grants Management and Scientific Review,  
NCATS

**Council Members**

Ronald J. Bartek, M.A.

Brad Margus, M.B.A.

Theodore R. Holman, Ph.D.

G. Lynn Marks, M.D.

Andrew W. Lo, Ph.D.

**Representative Members**

None present

**Ex Officio Members**

James B. Petro, Ph.D., M.S.S.I., Director, Human Systems Directorate, Office of the  
Undersecretary of Defense for Research and Engineering

Rachel Ramoni, D.M.D., Sc.D., Chief Research and Development Officer, Office of Research and  
Development, U.S. Department of Veterans Affairs (VA Research)

**Others Present**

Richard Dickinson, Ph.D., National Science Foundation (NSF)

Kiran Reddy, M.D., Blackstone Life Sciences

Michael Rosenblatt, M.D., Flagship Pioneering

Elizabeth Stoner, M.D., MPM Capital

Khaled Bouri, M.D., M.P.H. (for Stephen M. Hahn, M.D.), U.S. Food and Drug Administration  
(FDA)

NCATS leadership and staff

**I. CLOSED SESSION OF THE NCATS ADVISORY COUNCIL**

This portion of the Advisory Council meeting was closed to the public in accordance with the determination that it was concerned with matters exempt from mandatory disclosure under Sections 552b(c)(4) and 552b(c)(6), Title 5, U.S. Code, and Section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2).

Advisory Council members discussed procedures and policies regarding voting and the confidentiality of application materials, committee discussions and recommendations. Members did not participate in the discussion of and voting on applications from their own institutions or other applications in which there was a potential conflict of interest, real or apparent.

**II. ADJOURNMENT OF CLOSED SESSION OF THE NCATS ADVISORY COUNCIL MEETING**

Christopher P. Austin, M.D., adjourned the closed session of the NCATS Advisory Council meeting on September 17, 2020, at 11:56 a.m. ET.

**SEPTEMBER 17, 2020**

**III. CALL TO ORDER, OPEN SESSION DAY 1**

Dr. Austin called the meeting to order and welcomed members and guests to the 25th meeting of the NCATS Advisory Council. He noted that the meeting will consist of two sessions: Day 1, September 17, 2020, from 1:00 p.m. to 3:00 p.m.; and Day 2, September 18, 2020, from 11:00 a.m. to 3:00 p.m.

Dr. Austin reminded attendees that the open session was being webcast, introduced the members of the Council and previewed the meeting agenda. He also introduced the Cure Acceleration Network (CAN) Review Board members who are officially attending as guests in today’s meeting because of statutory requirements.

**IV. CONFIRMATION OF DATES FOR FUTURE MEETINGS: Anna L. Ramsey-Ewing, Ph.D., Executive Secretary, NCATS Advisory Council**

Anna L. Ramsey-Ewing, Ph.D., confirmed the schedule for the meetings of the NCATS Advisory Council and CAN Review Board for 2021 and 2022:

- January 14, 2021
- May 20, 2021
- September 23, 2021
- December 10, 2021 (CAN Review Board only)
- January 20, 2022
- May 19, 2022
- September 22, 2022
- December 9, 2022 (CAN Review Board only)

**V. APPROVAL OF MINUTES: Anna L. Ramsey-Ewing, Ph.D., Executive Secretary, NCATS Advisory Council**

Members unanimously approved the minutes from the May 2020 meeting.

**VI. CLEARANCE OF CONCEPTS**

The Council received presentations on six new projects and one renewal project that NCATS is considering for funding. At the end of each presentation, the members discussed the proposal and voted on whether to approve NCATS’ moving forward with the initiative.

**Small Research Grants for NCATS Clinical and Translational Science Award (CTSA) Program:  
Erica K. Rosemond, Ph.D., Deputy Director, CTSA Program Hubs, Division of Clinical Innovation (DCI),  
NCATS**

Erica K. Rosemond, Ph.D., presented a concept to establish small research grants within the CTSA Program. These grants will address the challenge of speeding up the clinical and translational science research process that typically takes multiple steps and time to deliver a solution to any single operational problem. To speed up this research process, NCATS is proposing small clinical and translational science research projects, which can be leveraged to advance science more quickly and identify “fast-fail” decision points in the project.

The objectives and emphasis will be that these small, self-contained research projects can (1) address general roadblocks in science or operations that limits the efficiency and effectiveness of translation, and (2) develop, demonstrate or disseminate innovative solutions or new or improved treatments that will have an impact on improving the health of patients. In addition, the small research grants will provide an opportunity to support the transition of clinical and translational scientists to achieve independent investigator status.

In implementation, these grants will help research support projects get over a roadblock, catalyze a tangible scientific outcome and allow projects to fail fast resulting in a change in approach. The overall impact will be assisting young (i.e., early-career) investigators in building their independent research portfolios and transitioning to careers as independent academic translational scientists.

***Discussion***

Theodore R. Holman, Ph.D., commented on how this concept would assist scientists in testing the feasibility of their research ideas and preliminary data. Recognizing that the budget of the small research grants would be a determining factor in deciding on the types of projects this concept could target, Dr. Holman suggested software development, data management and data science projects focusing on mining clinical trial data to provide insight on race and gender differences, as areas of emphasis. Dr. Ramsey-Ewing confirmed that the small research grants typically have a maximum budget of \$50,000.

Andrew W. Lo, Ph.D., expressed his enthusiasm for the concept, which is assisting early-career investigators in potentially achieving substantial funding, such as a first National Institutes of Health (NIH) R01 grant before reaching the average age of 40 years. From a financial and economic perspective, Dr. Lo suggested focusing on high-risk, high-return on investment projects for the small research grants. He elaborated on areas of research that are neglected because of a lack of either scientific expertise or industry focus and remarked on how NCATS is uniquely positioned to identify these intellectual “valleys of death,” which could be potential targets for the small research grants. Because one key aspect of this new program will be to stimulate new perspectives by adopting a fast-fail approach, Dr. Lo proposed including a mechanism (e.g., annual research conference) to disseminate the information regarding the projects and the research, which would benefit both the award recipients and the broader scientific community.

:: Rachel Ramoni posted in the Chat to all participants: What drove the demand for these small research grants? What would the application process/turnaround time look like?

Elizabeth Stoner, M.D., asked about plans to integrate the existing CTSA Program grants that support early-career investigators and how NCATS envisions transitioning the small research grants to a larger, robust CTSA funding structure. Dr. Rosemond explained that the small grants (e.g., R03s) will focus on the individual investigator rather than the large-scale efforts, such as the CTSA Program Collaborative Innovation Awards (CCIAs) currently available in the CTSA Program. Michael G. Kurilla, M.D., Ph.D., added that the new NCATS Small Research Grant Program (R03) will target early-career investigators focusing on clinical and longer-term translational research, enabling them to build their resumes and track records to become more competitive in securing academic tenure-track positions and/or NIH funding.

Dr. Rosemond clarified that the application receipt dates for the awards will be three times per year, with a standard turnaround time for NIH grants. Dr. Austin explained that a more rapid review process (e.g., Other Transaction Authority) had been considered but noted that a certain amount of non-compressible time would still have existed.

Rachel Ramoni, D.M.D., Sc.D., suggested a separate application review process and establishing a center within the CTSA Program to distribute the funds. Dr. Kurilla pointed out that each of the CTSA Hubs manages a pilot project program, which has funds available locally.

Michael Rosenblatt, M.D., expressed his support for the concept, which addresses a need for a forum in which ideas can be translated. He expressed concern that premature NIH funding could result in a gradual shift in objectives regarding the mission of NCATS and/or the CTSA Program. Dr. Rosenblatt emphasized focusing on one question for a research project, with a clear vision of a translational next step (e.g., clinical trial and/or partnership).

:: Rachel Ramoni posted in the Chat to all participants: I agree with the previous comment about sharpening the focus — is it for early investigators to get an NIH “win” on the board or for the “fail fast” ideas?

:: Christopher Austin posted in the Chat to all participants: @Rachel: it’s both, but the latter >> former, or perhaps, better stated, the latter leading to success of the former.

Kiran Reddy, M.D., asked about the possibility of including a mentorship component and increasing awareness about the research among experts in the field. Dr. Rosemond noted plans of soliciting applications for the R03s, in limited competition, among the CTSA institutional career development awards program (KL2) scholars, adding that the KL2 includes a mentorship component. The CTSA Program also has a robust communication infrastructure that could support convening grantees in a symposium.

Council and Board members noted efforts, initiatives or processes that could be modeled for this concept. G. Lynn Marks, M.D., called attention to the Easy Broad Agency Announcement (EZ-BAA), the rapid review process used in the Biomedical Advanced Research and Development Authority (BARDA). EZ-BAA, which supports breakthrough innovations, is designed to return a decision on funding (e.g., \$750,000 budget) within 30 days of an application’s being submitted. James B. Petro, Ph.D., M.S.I., further elaborated on the U.S. Department of Defense (DoD) seedling initiative supporting young investigators exploring nontraditional opportunities and focusing on high-risk, high-reward research not being funded elsewhere. Essentially, investigators within the DoD enterprise evaluate novel discoveries and technologies that could yield future military capabilities and are funded for 2-year research projects, with a budget of approximately \$750,000.

:: Ben Petro posted in the Chat to all participants: Are there examples of projects/opportunities in mind, or is the origin of the concept more along the lines of addressing shortfalls in opportunities for young investigators to access funds for applied studies?

Dr. Redmond explained that some of NIH's sister agencies have leveraged small research grants to stimulate young investigators who have progressed to additional funding and advanced their project. Within the NCATS portfolio, funded M.D.s and M.D.-Ph.D.s receive additional career development awards; this new concept is anticipated to further advance these individuals to larger, independent research grants. Dr. Kurilla remarked on one area in which a small research grant award would be productive: developing or validating technologies to support clinical trials.

Members unanimously approved the CTSA Program small research grants concept.

**Translational Ethics Collaboratories: Elaine Collier, M.D., Senior Advisor to the Director, Office of the Director, NCATS**

Elaine Collier, M.D., presented a concept of a translational ethics collaboratories program, a next phase in the NCATS ethics research program. Although novel discoveries and emerging technologies offer potential to improve health, the possibility for harm to health or to the norms of individuals, families and communities—as well as of society—remain. The goals of the concept are threefold: (1) support institution-independent collaborative transdisciplinary teams to conduct research on ethical, legal and societal issues related to the application of a novel discovery or emerging technology to improve health, (2) provide research ethics consultation outreach to the research community in a selected area of emphasis, and (3) collect data on this consultation model.

The collaboratory area of emphasis (e.g., synthetic biology, gene modification or data aggregation) must present an ethical issue involved in translation and requires a research consultation project. NCATS is the only NIH Institute or Center that targets systemic issues agnostic of disease, specialty or age across the entire research spectrum, from basic and clinical research to research focused on health care and public health. The translational ethics collaboratories will fill a gap in the knowledge and practice necessary to advance novel discoveries to improve human health in emerging areas. NCATS anticipates that the collaboration of translational scientists, ethicists, legal scholars and social scientists becomes comfortable and routine and facilitates interdisciplinary translational ethics research and consultation. The outcome will provide evidence on the usefulness of research ethics consultation and the effectiveness of models.

***Discussion***

Drs. Lo and Marks expressed their support of the concept, which is unique in its approach of bringing the research community together to focus on ethical considerations, including systemic issues. Dr. Lo asked about ways to increase awareness (e.g., workshops or targeted proposals) of the program to engage the relevant stakeholders, plans to involve compliance officers at research institutions and whether discussions on the ethics of human challenge trials had been considered. Dr. Collier pointed out that outreach to the translational research community will be an important component of the research ethics consultation, which could be expanded to include institutions but not necessarily compliance officers. She commented that ethics and human challenge studies, which have been significant issues that surfaced in Ebola studies and recently with COVID-19 regarding moving technology to clinical application, can be an area of emphasis to include in this concept.

Dr. Marks commended NCATS for not proposing to serve as the NIH ethics review center, but rather stimulating research on how to conduct these reviews using a consultative, collaborative and interoperable model of expertise. He suggested that further discussion of the roadmap on how NCATS is viewing such an ethics research consultation program be a future agenda topic for the Council and Board. From his perspective, human challenge studies would be a welcomed, but in-depth, area of emphasis to consider reviewing due to the decisions being made having the potential to harm even one individual.

:: Rachel Ramoni posted in the Chat to all participants: NCATS does a wonderful job of engaging the communities impacted by research/patient communities. How would they be involved?

:: Michael Rosenblatt posted in the Chat to all participants: Are there other ethics committees across NIH and, if so, would this program potential arrive at different ethics guidance than other NIH committees?

Dr. Collier clarified that this new program would focus on connecting research communities (e.g., translational groups and computational scientists) that lack research ethics consultation, but it would not be developing answers or guidance on ethics. The advent of neuroscience studies, specifically brain research evaluating consciousness in pig brain, is one example of an area that needed consultation early on. Dr. Collier added that ethics and clinical research issues have been and remain a focus of the NIH Clinical Center and extend to the Brain Research through Advancing Innovative Neurotechnologies® (BRAIN) Initiative. Other groups, such as the national clinical ethics consultation community, share this expertise.

:: Rachel Ramoni posted in the Chat to all participants: I'll put a plug in for the Undiagnosed Diseases Network as a place for this work, as there you have patients, basic scientists, and clinicians working together. Will also need to clearly define whether animal research ethical concerns are within or out of scope.

Dr. Collier agreed that the Undiagnosed Diseases Network (UDN) would be optimal for this concept and noted that NCATS envisions including animal research issues, as well as others involving translational discoveries.

:: Ben Petro posted in the Chat to all participants: This is an exciting and timely concept that can bridge the gap between the predominantly policy-level frameworks developed by NAS (National Academy of Sciences) and others and the need for a discrete researcher-focused framework to help them understand and work through potential ethical issues and risks from moving a concept or technology into a living system. Concur that this should include animal use as well as human.

Dr. Petro highlighted DoD's efforts in addressing ethical questions, including a Defense Advanced Research Projects Agency ethics team's examining issues before approving research projects and an ethical, legal and societal issues group that informs biotechnology programs. He elaborated on ethical issues of impact in the war-fighting space regarding technology application and conducting clinical trials evaluating genetic and biological indicators of performance. He suggested closing the gap in ethics and policy by resourcing investigators to study cutting-edge technologies advancing into the translational space.

:: Christopher Austin posted in the Chat to all participants: We clearly need to allow more time for our concept clearances. The first two discussions are exactly what we need for all concepts, and each of

them will be quite different because of your input. We have to stay within time today, but we will allow more time in the future.

Members unanimously approved the translational ethics collaboratories concept.

### **Introduction of Office of Rare Diseases Research (ORDR) Concepts: Anne R. Pariser, M.D., Director, ORDR, NCATS**

Anne R. Pariser, M.D., introduced and provided a brief background on three of the four new ORDR concepts that focus on rare disease informatics and knowledge management. Approximately 25 to 30 million people in the United States are living with rare diseases, the majority of which lack effective treatments, and these people face a long diagnostic odyssey (i.e., journey) to their diagnosis. More than 7,000 different rare diseases have been identified, but accurate, reliable and objective information is lacking; although the available information about rare diseases is steadily increasing, managing this information can be challenging. Identifying rare disease patients in existing health care system databases is difficult, and rare diseases remain under-recognized, undercounted and underdiagnosed or misdiagnosed — all of which results in an underestimation of the of the true magnitude of the rare diseases public health dilemma. Dr. Pariser noted the overall need that the ORDR is seeking to address developing reliable and objective approaches to information management, including a translational science rare disease database, that can be scalable across rare diseases. The ORDR is proposing one concept renewal and two new concepts to address the rare disease informatics problem, leveraging existing NCATS informatics programs.

### **Genetic and Rare Diseases (GARD) Information Center: Eric Wk Sid, M.D., M.H.A., Program Director, ORDR, NCATS**

Eric Wk Sid, M.D., M.H.A., presented a renewal concept for the GARD Information Center. GARD was launched in response to the Rare Diseases Act of 2002 and congressional mandate to provide consumer health information on rare diseases. Over the past 5 years, the demand for information— with contact center inquiry volume doubling and research evidence exponentially increasing — has outpaced GARD staff's capabilities to manually maintain and expand content. The GARD Information Center currently is the most visited NCATS webpage, and the traffic (2 million users per month) has at times paralleled that of the NIH home page.

The goal of this concept renewal is to modernize the GARD program and enhance NCATS' public health role in delivering reliable information about rare diseases to patients and caregivers. The objectives will be to sustainably audit research on the more than 7,000 current and newly identified rare diseases and enhance the ability of GARD to be of maximum use to patients and caregivers. The key areas of emphasis include developing both a research dashboard to quantify and visualize the research evidence in the rare disease portfolio and a translational science framework to educate consumers on rare disease evidence interpretation. A total of 34 public datasets comprising 3.8 million data points are now integrated into GARD's database from existing NCATS programs and other rare diseases resources. In this next phase, efforts will focus on investigating translational science approaches to leverage these data.

NCATS anticipates that this GARD modernization will clear the contact center's inquiry backlog by automating processes to stay abreast of new research findings and improve the ability of rare disease

patients and caregivers to make decisions using these data, with the outcome of shortening the diagnostic journey for patients with rare diseases.

### ***Discussion***

Ronald J. Bartek, M.A., expressed his support for the concept, which will fully update and upgrade the GARD Information Center to a digital platform. He asked about similar upgrades ongoing in other NIH Institutes and Centers (ICs) and across rare diseases and whether the Toolkit for Patient-Focused Therapy Development (Toolkit) and Rare Diseases Registry Program (RaDaR) contributed to the GARD website visits. Dr. Sid explained that data from the National Library of Medicine has been integrated into GARD and noted that the initial informatics approach will be to identify the existing data sources for the 7,000 known rare diseases, which likely reside on customizable platforms, and then to connect the other terminologies (e.g., International Classification of Disease codes) and data. Dr. Sid pointed out that both the Toolkit and RaDaR are resources designed for specific groups and would be challenging to include them in GARD's website analytics.

In response to a question from Dr. Ramoni about a separate information link for clinicians in GARD, Dr. Sid noted that the research dashboard being developed will contain data useful to clinicians and researchers on the issues common across all rare diseases.

Members unanimously approved the GARD information center concept.

Dr. Ramsey-Ewing noted a change in the order in which the concepts will be presented: the fourth concept will be Scanning for Conditions with Electronic Nose Technology (SCENT) and the seventh concept will be Bespoke Gene Therapy Consortium (BGTC) Coordinating Center.

### **Office of Special Initiatives, Concept**

**Scanning for Conditions with Electronic Nose Technology (SCENT): Danilo Tagle, Ph.D., M.S., Associate Director for Special Initiatives, Office of the Director, NCATS; Leah Tolosa Croucher, Ph.D., Program Officer, Office of Special Initiatives, Office of the Director, NCATS**

Danilo Tagle, Ph.D., M.S., presented the SCENT concept. The goal is to develop a noninvasive and portable diagnostic device that provides rapid and accurate diagnosis of a variety of medical conditions, facilitating treatment of patients. The most pervasive method of sensing in nature, detection of scents and odors, has scarcely been used in the diagnosis of disease. This concept aims to reverse engineer a bio-mimic of the sense of smell found in canines for disease diagnostics, involving several steps — from the detection of the smell/odor, to data acquisition and processing, to comparisons of known patterns, and the readout via a mobile device or portable system.

Leah Tolosa Croucher, Ph.D., explained that the objectives of the concept are to use volatile organic compounds (VOCs) that are released through the skin and/or breath as the key substrate, integrate the components of the various SCENT instrumentation and software, and establish VOC signatures unique for each disease. The SCENT devices will adhere to the Affordable, Sensitive, Specific, User-friendly, Rapid and robust, Equipment-free and Deliverable to end users (ASSURED) criteria outlined by the World Health Organization (WHO). Machine learning and artificial intelligence will be incorporated to rapidly analyze the VOC signatures unique for each disease and condition, and to ensure that the WHO ASSURED criteria are met.

The anticipated result would be a market-ready handheld/wearable, noninvasive diagnostic device that is expected to decentralize diagnostic testing, bringing it closer to patients and resulting in improved care and patient outcomes.

### ***Discussion***

Dr. Holman remarked on the SCENT program as an ideal area for NCATS to explore and suggested ongoing improvements to the detection method and enhancing the SCENT platform over time by expanding the VOC set. One key to success would be to align the hardware, software and clinical experts in synthesizing the data. With a small seed grant to scan for COVID-19 to start-up this initiative, Dr. Tagle anticipates that lessons learned will lay the foundation for detecting other diseases.

Dr. Marks expressed his enthusiasm for the concept and noted the need to connect with existing groups across the federal government doing this type of research, such as BARDA's Division of Research, Innovation, and Ventures program and its Early Notification to Act, Control, and Treat program, which focuses on wearables and VOCs. He recommended rapidly transmissible infectious diseases as an area of emphasis. Dr. Tagle noted ongoing efforts in partnering with DARPA on its existing electronic nose (e-Nose) technologies focusing on infectious diseases.

When asked which diseases are likely to be most effective with SCENT, Drs. Croucher and Tagle identified diabetes mellitus (which involves continuous monitoring) and cancer, both of which have unique VOCs. Epilepsy, metabolic diseases and infectious diseases also are other areas to investigate.

Members unanimously approved the scanning conditions for e-Nose technology concept.

### **ORDR Concepts (continued)**

#### **Novel Explorations in Rare Diseases (NERD): Anne R. Pariser, M.D., Director, ORDR, NCATS**

Dr. Pariser presented the novel explorations in rare diseases concept and noted the rationale for such a program. Extracting rare disease patient information from existing health care system databases is exceedingly challenging and often unreliable. The available tools are not readily usable for rare diseases, especially multi-disease explorations/analyses. Data extraction is unique to individual data environments (e.g., electronic health record (EHR) system, region/location). NCATS is proposing this concept to quantify the impact, including cost and health care utilization, of rare diseases on patients and health care systems.

The objectives are threefold: (1) develop methodology to accurately and broadly estimate the prevalence of rare diseases and associated health care utilization, (2) develop patient journey maps across different diseases to objectively describe and quantify the diagnostic odyssey and (3) adapt machine learning software and tools to derive this information directly from primary source data. Key focus areas include identifying, with reproducibility, patients with rare diseases within different health care databases, quantifying the overall impact, and working with partners and/or vendors to develop the necessary methodology and tools.

Regarding implementation, a NERD 14-disease pilot is being conducted intramurally, and some efforts are in progress externally with academic and industry partners in the United States and Western Australia. NCATS envisions this concept as having the transformative potential to improve

understanding of the magnitude of rare diseases and their impacts on the health care and research systems and on the well-being of patients and their survival.

### ***Discussion***

Brad Margus, M.B.A., asked whether the main purpose is to build a better case to convince the public that rare diseases are important or whether it is a matter of framing the message. He noted that a concept of this level could provide an added benefit for patients by addressing obstacles to access data owned by pharmaceutical companies or found in insurance claims and/or prescription records.

Dr. Pariser explained that this concept will be addressing high research needs, focusing on extracting patient data from available health care systems and evaluating underlying patterns to accelerate a rare disease diagnosis.

In response to queries from Mr. Bartek on the availability of data from the pilot study and whether the concept will provide insight on the proportion of the disease burden attributable to a specific therapy, Dr. Pariser explained that plans are to disseminate preliminary data from the pilot when they are made available. She noted that NCATS is up-to-date on the various types of disease burden determinations and is partnering with patient advocacy groups (PAGs) on this topic. A major goal of this concept is to develop a reproducible, shareable and easily interpreted methodology with broad application in the rare diseases community.

Members unanimously approved the novel explorations in the rare diseases concept.

### **Rare Diseases Informatics Platform (RDIP): Anne R. Pariser, M.D., Director, ORDR, NCATS**

Dr. Pariser presented a concept to establish a rare diseases informatics platform, which builds on the NCATS GARD and NERD proposals. This concept will address several needs. First, most rare disease information routinely used are estimates and are not easily traceable back to the primary data sources. Second, current data analysis efforts are discrete, siloed and do not comprehensively meet the prerequisite for timely rare diseases information. Third, the ability to collect and integrate rare disease information from multiple sources (e.g., insurance, EHR or research) is lacking. To address these needs, NCATS proposes this concept to support the collection, integration and analysis of rare diseases data from diverse sources. This information will inform NCATS' rare diseases research initiatives and priorities.

The objectives are to create and staff an RDIP or knowledge center; collect, integrate and analyze rare diseases data from diverse sources to provide objective information for multiple purposes; and incorporate ongoing ORDR data initiatives within one central location. NERD is being designed as a model for building the RDIP, which will harmonize approaches or data models to integrate with or leverage other ongoing NCATS informatics programs, such as GARD, DCI-data initiatives and the Biomedical Data Translator.

### ***Discussion***

Mr. Bartek suggested including PAGs as sources of information and incorporating updated informatics from other NIH ICs. He asked whether this approach would be applicable to the early diagnostic value of newborn screening. Dr. Pariser replied that as the RDIP is built and its capabilities developed, it would enable incorporating data from multiple sources, including patients. Increasing understanding into the diagnostic journey likely will provide insight into diagnosis for newborns.

In response to a question from Mr. Margus on the ramifications of not establishing a RDIP, Dr. Pariser noted that this concept expands NERD to address a broader range of questions.

:: Ben Petro posted in the Chat to all participants: RDIP will have a dependency on NERD's success. Would it make sense to revisit this concept once NERD has demonstrated progress?

Although no progress of NERD is available at this meeting, Dr. Pariser confirmed that the concept of such a small and nimble program is unequivocally possible. She noted that data are being received and emphasized that any delay would impede building and capturing ongoing informatics needed.

Members unanimously approved the rare diseases informatics platform concept.

**Bespoke Gene Therapy Consortium (BGTC) Coordinating Center: P.J. Brooks, Ph.D., Program Officer, ORDR, NCATS**

P.J. Brooks, Ph.D., presented a concept on the BGTC Coordinating Center. Many monogenic rare diseases could benefit from gene therapy using adeno-associated virus (AAV) vectors. For diseases of no commercial interest, navigating the multiple steps (e.g., vector production and toxicity testing) necessary to get to a clinical trial, as well as the clinical trial itself, is a major challenge. To address this challenge, NCATS, the FDA Center for Biologics Evaluation and Research, and the Foundation for the NIH (FNIH) are establishing the BGTC, a major component of the FNIH Gene Therapy Accelerated Medicines Partnership (AMP).

NCATS proposes a BGTC Coordinating Center to support these multiple steps using contract mechanisms, all under the direction of the Coordinating Center. The objectives are to coordinate contract activities for the BGTC and evaluate novel collaborative approaches to support gene therapy clinical trials for rare diseases. In addition to accelerating rare diseases clinical trials, other areas of emphasis for this concept include collaboration with multiple stakeholders (e.g., FDA, private industry, nonprofits and rare diseases PAGs) and commitment to ensuring that the diseases chosen for study will include those affecting racial and ethnic minority populations.

The BGTC Coordination Center and its activities are expected to be synergistic with other NCATS programs and initiatives, such as the Platform Vector Gene Therapy (PaVe-GT) project. In the long-term, knowledge gained and best practices will be parlayed into the AAV-based gene therapy clinical trials for rare diseases handbook and broadly disseminated.

***Discussion***

Mr. Bartek commended NCATS for coordinating multi-stakeholder engagement to accelerate gene therapy clinical trials in rare diseases despite little to no commercial benefit.

Mr. Margus sought clarity on what NCATS would be funding with this concept. Dr. Brooks clarified that the concept would support five to six gene therapy trials, each investigating a different rare disease, as well as the related activities, such as virus manufacturing and toxicity testing. The contract mechanism will be utilized.

Members unanimously approved the BGTC Coordinating Center concept.

**VII. ADJOURNMENT DAY 1: Christopher P. Austin, M.D., Director, NCATS, Chairperson, NCATS Advisory Council**

Dr. Austin adjourned Day 1 of the meeting at 3:45 p.m. ET.

**SEPTEMBER 18, 2020**

**VIII. CALL TO ORDER, OPEN SESSION DAY 2**

Dr. Austin called the meeting to order and welcomed members and guests to the second day of the 25th meeting of the NCATS Advisory Council. He reminded attendees that the open session was being webcast and reviewed the agenda.

**IX. DIRECTOR'S UPDATE: Christopher P. Austin, M.D., Director, NCATS, Chairperson, NCATS Advisory Council**

Dr. Austin began by expressing his appreciation to Todd B. Sherer, Ph.D., Chief Executive Officer, Michael J. Fox Foundation for Parkinson's Research, who recently completed his 4-year term as a member of the Advisory Council and CAN Review Board. Dr. Austin gave a brief update on the fiscal year (FY) 2021 budget, ongoing programs and other NCATS activities.

**Budget Update**

Dr. Austin pointed out that the FY 2020 budget ends September 30, 2020, and briefly noted the NCATS FY 2020 enacted budget total appropriations. The Council was reminded that the President's FY 2021 Budget proposal, released on February 10, 2020, included appropriations for the NIH and NCATS below the FY 2020 enacted budgets. The House congressional hearing occurred on March 4, 2020, but the Senate hearing was postponed because of COVID-19. The House passed a minibus spending bill on July 29, 2020, which includes a \$7.2 million increase for NCATS. The Senate has yet to pass its bill. A continuing resolution is likely to fund the government starting October 1, 2020. Congress approved four supplemental aid packages to address COVID-19, including the Coronavirus Aid, Relief, and Economic Security (CARES) Act, which appropriated \$36 million to NCATS. The House and Senate are still deciding on a fifth supplemental funding bill.

**Health Disparities Action Plan**

In response to the national discussions on race, Dr. Austin and the Office of Policy, Communications and Education (OPCE) actively have been developing a health disparities action plan. Health disparities crosscut many translational science problems. Dr. Austin emphasized that, since its beginning, one of the principles of NCATS has been to ensure that the diagnostics, therapeutics and interventions that improve human health are available to all patients who need them. The objective of this plan is to develop a framework to guide NCATS' activities focused on scientific workforce development and address health disparities. The NCATS Civility Council will focus on implementation and the OPCE Education Branch, on training programs. NCATS will conceptualize and implement new approaches to health disparities across scientific programs.

**NCATS Mission and Program Updates**

Although urgent public health crises (e.g., opioid addiction and coronavirus) have dominated the attention of the research community in the past 2 years, Dr. Austin assured the Council that the system-

wide, disease-agnostic NCATS mission focusing on getting more treatments to more people more quickly is continuing. The fact remains that the discordance between basic science findings and clinical application has significantly increased. Other diseases have continued to affect people, some leading to death. NCATS is playing an important role in the response to the Helping to End Addiction Long-term<sup>SM</sup> Initiative or NIH HEAL Initiative<sup>SM</sup> and COVID-19; both illustrate the problems NCATS addresses. Dr. Austin provided an update on other mission-related initiatives.

- **Rare Diseases Are Not Rare! Challenge 2.0.** NCATS sponsored the Rare Diseases Are Not Rare! Challenge 2.0, with the goal of changing the perception of the health and societal importance of rare diseases as a public health problem. The Challenge competition solicited submissions on creative ways to spread the message about the collective population prevalence of rare diseases and their health impact, using any art or media platform. Challenge 2.0 emphasized team collaboration, and the total prize was \$5,000. NCATS awarded first, second and third place prizes and five honorable mentions. Dr. Austin highlighted the first place submission “Keep on Fighting,” a spoken-word poetry video by Mr. Jacob Thompson. Details on all winning submissions and honorable mentions can be accessed from the [NCATS Rare Diseases Are Not Rare!](#) website.
- **NCATS Platform Vector Gene Therapy (PaVe-GT).** Dr. Austin reported that the many-diseases-at-a-time approach, PaVe-GT, is being used to test a commonality present in two rare diseases: Hermansky-Pudlak syndrome (HPS), a rare genetic disorder, which may lead to pulmonary fibrosis (PF) and Prader-Willi syndrome (PWS), a rare genetic disorder characterized by hypogonadism, developmental delay and hyperphagia. In animal models, cannabinoid receptor type-1 (CB1R) antagonists reduce both PF in HPS and hyperphagia in PWS. NCATS collaborator and intramural senior investigator Dr. George Kunos and his laboratory in the National Institute on Alcohol Abuse and Alcoholism developed a novel CB1R antagonist, MRI-1867, a non-brain penetrant with minimal neuropsychiatric side effects. NCATS is developing MRI-1867 for HPS-PF and Inversago Pharma for PWS. NCATS will conduct long-term safety and toxicology studies to support phase 2 studies in both PWS and HPS.

### **NIH HEAL Initiative<sup>SM</sup>**

Dr. Austin remarked on the worsening of the opioid crisis during the COVID-19 pandemic. The rate of untreated addiction and overdose has dramatically increased over the past 6 to 8 months, emphasizing that the need for the NIH HEAL Initiative remains urgent. NCATS is leveraging the capabilities of Division of Preclinical Innovation (DPI) programs to develop human-based testing platforms predictive of human response and to perform drug development. Dr. Austin provided updates on NCATS’ preclinical HEAL programs, highlighting projects centered in the Tissue Chips and Drug Development programs.

- **Tissue Chips to Model Nociception, Addiction and Overdose.** NCATS awarded five research grants in this category: to the University of Texas, Dallas, for “Human-Induced Pluripotent Stem Cell-based Dorsal Root Ganglion Tissue Mimics on Multi-well Microelectrode Arrays as a Tissue Chip Model of Acute and Chronic Nociception”; to Tulane University for “Human Microphysiological Model of Afferent Nociceptive Signaling”; to the University of Pittsburgh for “Joint Pain on a Chip: Mechanistic Analysis, Therapeutic Targets, and an Empirical Strategy for Personalized Pain Management; to the University of Central Florida for “Multi-Organ Human-on-a-Chip System to Address Overdose and Acute and Chronic Efficacy and off-target toxicity”; and to Hesperos in the University of California, Los Angeles, for “Multi-Organ-on-Chip Device for

Modeling Opioid Reinforcement and Withdrawal, and the Negative Affective Component of Pain: A Therapeutic Screening Tool.”

- **Development of Investigational New Drugs for Clinical Testing.** Dr. Austin explained that Dr. Amy Hauck Newman at the National Institute on Drug Abuse is collaborating with Braeburn, Inc., to develop selective dopamine D3 receptor (D3R) antagonists for treating opioid use disorders (OUD). A lead candidate D3R antagonist, VK4-116 —which is effective in animal models of OUD but does not affect blood pressure, heart rate, or locomotor activity or activation and does not reduce opioid analgesia — is being further evaluated. NCATS is supporting the project through preclinical development through an FDA IND application and onto clinical trials. Good manufacturing practices and the manufacturing process have been optimized. Safety assessments are in progress, and a back-up lead series compound is being developed.

Dr. Austin updated the Council on NCATS clinical NIH HEAL Initiative<sup>SM</sup> programs.

- **Pain Management Effectiveness Research Network (Pain-ERN).** The goal of the Pain-ERN is to compare the effectiveness of existing therapies or ways to deliver current therapies to inform clinical treatment guidelines for acute and chronic pain. Four Pain-ERN trials have launched in collaboration with four different NIH ICs. The NCATS Trial Innovation Network (TIN) is providing data, clinical and biostatistical coordination, and support for study recruitment. All four trials met their milestones and have been approved to advance from the planning phase to trial implementation. Trial design changes due to COVID-19 had to be incorporated; two studies are using fully remote methods, and the remaining two are minimizing in-person visits and maximizing remote methods to the fullest extent possible. The Pain-ERN has been approved to open a fifth trial, likely to begin planning in October 2020.

## COVID-19 Updates

Dr. Austin updated the Council on NCATS’ response to COVID-19, including support functions, serology research and clinical trials. He explained that the NIH Return to the Physical Workspace plan is in progress for the Intramural Research Program and 32 percent of staff have returned onsite. Safety practices, including social distancing and wearing a mask, are being maintained.

- **Office of Grants Management and Scientific Review (OGMSR).** To support the extramural community during the COVID-19 pandemic, OGMSR issued first-of-its-kind funding opportunity announcements for new urgent awards, designed and developed policy and operations packages for emergency and urgent awards and developed, and implemented and disseminated a new approach to conflict of interest management for merit evaluation of COVID-19 applications. The Office of Scientific Review accelerated review of COVID-19 applications and conducted the first objective review of emergency grant applications under COVID-19 rules.
- **NCATS OpenData Portal.** The DPI developed an OpenData Portal, which is providing a translational science solution to publicly share data and information on NCATS SARS-CoV-2 assays, drug-screening efforts and protocols.
- **CURE ID.** The DCI and FDA co-developed CURE ID, a mobile application (app) allowing certified health care professionals to share their clinical experience on using approved drugs to treat diseases other than the one for which they are regulatorily indicated. [CURE ID](#) launched on December 5, 2019, and can be accessed from the NCATS website or downloaded as the mobile app.

- **SARS-CoV-2 Serosurvey.** The DPI, in collaboration with the National Institute of Biomedical Imaging and Bioengineering, National Institute of Allergy and Infectious Diseases and National Cancer Institute (NCI), initiated a serosurvey. This study, which will inform guidelines on virus infection and spread, is evaluating the proportion of the healthy population that has been exposed to SARS-CoV-2 infection by measuring antibodies in blood serum using a robust in-house assay. To date, 10,000 healthy volunteers have been recruited in collaboration with the CTSA Program Hubs, and more than 8,500 samples analyzed.
- **Biomedical Data Translator (Translator).** Dr. Austin described an example of the utility of Translator tool-enabled research to rapidly advance from target identification to a clinical trial. NCATS-supported Translator investigators, Drs. William Byrd and Matthew Might, at the University of Alabama at Birmingham (UAB) bisphenol A, an estrogen, reduced the expression of transmembrane protease, serine 2, a SARS-CoV-2 spike protein activator. The investigators formulated a testable hypothesis that anti-androgens FDA-approved for prostate cancer could treat COVID-19 and provide insight into the finding of increased morbidity and mortality in men compared with women. A phase 2 clinical trial — Hormonal Intervention for the Treatment in Veterans with COVID-19 Requiring Hospitalization (HITCH) — in collaboration with the VA, was launched.
- **Tissue Chips in COVID-19.** NCATS-funded investigators at the Wyss Institute used their lung-on-a-chip model to study viral entry of SARS-CoV-2 and test potential drugs. In a proof-of-concept study, the researchers identified drugs effective in inhibiting viral infection, suggesting that tissue chips can help identify existing drugs that may be repurposed for pandemic viral applications.
- **Rare Diseases Patient Impact Survey.** On May 1, 2020, the ORDR — through the Rare Diseases Clinical Research Network (RDCRN) — launched a voluntary, online survey (with English and Spanish versions) to obtain objective data to assess the impact of COVID-19 in the rare diseases community. More than 3,500 surveys have been completed either by patients or primary caregivers from across all 50 states and Puerto Rico, spanning more than 130 different rare diseases.
- **National COVID Cohort Collaborative (N3C).** NCATS' DCI and Information Technology Branch developed the N3C to collect and make available vast amounts of clinical data from EHRs to speed up COVID-19 research and improve patient care. A centralized but not federated data model, N3C is a secure enclave that provides access to EHR data from people diagnosed with COVID-19 across the United States. N3C leverages the existing resources of the CTSA Program Hubs and Center for Data to Health (CD2H); is unique in scale and scope, data harmonization and collaborative analytics; and is built into NCATS' secure cloud, FedRamp. The N3C data enclave opened for research on September 3, 2020, and contains data from nearly 500,000 patients, 59,000 of whom have received a COVID-19 diagnosis.

### ***Discussion***

When asked whether the House budget lists appropriations for the CAN, Dr. Austin replied that no indication had been given as to what the CAN budget would be, but noted that the congressional justification conveyed NCATS' requests in this area.

**X. PROGRAM UPDATE: DIVISION OF CLINICAL INNOVATION: Michael G. Kurilla, M.D., Ph.D., Director, Division of Clinical Innovation (DCI), NCATS**

Dr. Kurilla presented an overview of DCI that included updates on the CTSA portfolio activities, trans-NIH activities and efforts addressing COVID-19 research.

**CTSA Portfolio Activities**

Dr. Kurilla described existing CTSA networks and new awards funded in FY 2020 throughout the United States, explaining that most support is provided in areas with highest population density.

- **CTSA Program Collaborative Innovation Awards** focus on collaboration among CTSA Hubs. The U01 grants consist of three or more CTSA Hubs, and R01 grants require only two CTSA Hubs. NCATS issued 12 CCIs encompassing 53 institutions, all aligning with the NCATS strategic plan. The Accelerate Translational Advancement for Patients with Intellectual and Developmental Disabilities: Leveraging Clinical Genomics project based at Washington University in St. Louis involves several CTSA Hubs, and the Intellectual and Developmental Disabilities Research Center at the *Eunice Kennedy Shriver* National Institute for Child Health and Human Development. The aim of this project is to use genomic data to inform the science associated with brain developmental and behavior.
- **The CTSA Limited Competition, Competitive Revision Award** is a mechanism to support distributing tools developed at one institution broadly across the CTSA program. In FY 2020 UAB received funds for dissemination of its I-Corps™ methodology, which helps researchers evaluate their discoveries for commercial potential. The NSF's original design for I-Corps™ was successfully adapted and used across the NIH.
- **The CTSA Diversity and Re-Entry Research Supplements** support diversity and provide a pathway for re-entry to the scientific workforce. The CTSA Program webpage includes awardee profiles showing their activities and indicating how the award is affecting their success. Dr. Kurilla acknowledged the FY 2020 awardees and remarked on how the diversity supplements are helping to advance the careers of awardees. For example, Aisha Langford, Ph.D., M.P.H., Assistant Professor, Department of Population Health, New York University (NYU) Grossman School of Medicine, who received the award in 2016 to investigate the use of recruitment support tools now focuses on health communication, improving decision-making and reducing health disparities — work that is especially important in relation to COVID-19. Dr. Langford codirects the NYU Clinical and Translational Science Institute (CTSI) Recruitment and Retention Unit.
- **The CTSA Consortium Steering Committee** added members in FY 2020 and reconfigured the way the committee focuses on specific working groups. The CTSA Visiting Professorship Working Group allows young investigators to gain specific experience and expand their networks to foster the future exchange of ideas among CTSA Hubs. The Advancing Dissemination and Implementation Sciences in the CTSA Working Group focuses on how to better integrate and disseminate scientific tools across the CTSA program.
- **Request for Information (RFI): Enhancing the Clinical and Translational Science Awards (CTSA) Program.** On September 1, 2019, NCATS issued an RFI to solicit input from stakeholder communities on ways the Program could be strengthened. More than 100 comments were

received from diverse sources (e.g., academia, advocacy groups and integrated health solutions groups) Responders noted several areas of improvement for the CTSA Program, encompassing increasing flexibility and diversity across the Hubs; sharing best practice tools and materials; developing uniform guidance for research, training and education; standardizing data collections; enhancing reward teams; expanding funding opportunities; and simplifying the funding opportunity announcement.

### **Administrative Updates and Outreach**

Dr. Kurilla announced that the former director of the CTSA Program, Mary Purucker, M.D., Ph.D., who recently retired, has returned to the DCI as a contractor. The DCI welcomed new program directors with a broad range of expertise in FY 2020, some of whom were introduced at the May 2020 Council meeting. New program analysts and staff support also joined the DCI. Dr. Kurilla informed the members that Lindsey Criswell, M.D., M.P.H., a former CTSA multiple principal investigator at the University of California, San Francisco will be joining the NIH as the new Director of the National Institute of Arthritis and Musculoskeletal and Skin Diseases. Regarding outreach, the fall CTSA Program meeting is planned for November 18–20, 2020, and will be virtual.

### **Trans-NIH Activities**

Dr. Kurilla reported that the CTSA community has been very competitive in the trans-NIH programs in collaboration with other NIH ICs, and he provided an update on two of those activities.

- **The *All of Us* Research Program** requested CTSA assistance with its participation in the N3C.
- **Trans-NIH Research Focused on Maternal Mortality.** The CTSA community received 11 awards to combat rising maternal mortality rates in the United States. One award funded the Implementing a Maternal Health and Pregnancy Outcome Vision for Everyone (IMPROVE) project, which focuses on maternal mortality in Georgia. Data from the IMPROVE project will be used to identify drivers of maternal mortality, including social determinants of health and linguistic and cultural barriers.

### **Addressing COVID-19 Research**

Many CTSA activities have been directed toward investigating the utility of convalescent plasma as a treatment for hospitalized COVID-19 patients.

- **Convalescent Plasma to Limit COVID-19 Complications in Hospitalized Patients Trial (CONTAIN COVID-19).** Two CTSA Hubs, NYU and Albert Einstein University, launched the CONTAIN trial evaluating the use of convalescent plasma treatment and enrolled the first patient in April 2020, with the initial enrollment target of 300 patients. Additional sites will be activated to accelerate accruals, with a target of 1,000 patients per site. The University of Texas in Houston will add six sites in Texas, University of Miami will add two sites in Florida, and Yale University will contribute data from sites in Connecticut.
- **Passive Immunity Trial of the Nation for COVID-19 (PassItOnII).** Vanderbilt University started the PassItOnII trial, coordinated by CTSA, which enrolled 59 patients. Additional sites will be added to the trial with the provision of additional funding.

- **NYU Hub and CTSI: COVID-19 Frontlines.** The NYU CTSI, a funded CTSA Hub, has been on the COVID-19 frontlines. Dr. Kurilla elaborated on one example of an NYU resident physician, postdoctoral fellow and CTSI co-researcher, Gillian Baptiste, M.D., pivoting to the frontlines of COVID-19 clinical research activities. After being left without a laboratory to conduct her basic research because of the COVID-19 closures, Dr. Baptiste became the enrollment coordinator for two of the NYU clinical trial sites and has shifted her focus to clinical research as a CONTAIN COVID-19 sub-investigator.
- **SARS-CoV-2 Pandemic Serosurvey and Blood Sampling Study.** The University of Pittsburgh and UAB Hubs were critical for donor recruitment and sample acquisition in support the serosurvey study previously described by Dr. Austin. collectively, the CTSA Hubs contacted more than 400,000 respondents to obtain information that epidemiologists used to select 10,000 samples from these respondents to determine COVID-19 seroprevalence in people of various ages and geographic, racial and ethnic backgrounds. The NCI has taken the lead in serologic analysis and has approved the CTSA for 6- and 12-month follow-ups for this population.
- **N3C and Seroprevalence Data.** As of September 7, 2020, NCATS executed 58 data transfer agreements and 39 data use agreements across the CTSA and incorporated data from 12 CTSA Hubs. Currently, 15 sites are contributing a large amount of seroprevalence data, which can be used to address many questions about COVID-19. Linking other public data sets is planned.
- **Accelerating COVID-19 Therapeutic Interventions and Vaccines Master Protocol 1 (ACTIV-1).** The CTSA Program and TIN have partnered to lead the ACTIV-1 clinical trial assessing the efficacy and safety of immunomodulators as a supplementary treatment for hospitalized COVID-19 patients. Enrollment is projected to start in October 2020 and will involve at least 45 U.S. sites and 15 international sites. COVID-19 projects received regular FY 2020 funding and CARES funding — 47 awards to 26 CTSA Hubs. The N3C funding component supports data transfer.
- **The Recruitment Innovation Center (RIC),** an organizational partner on the NCATS TIN, has provided clinical trial recruitment support across the NIH since the onset of the COVID-19 pandemic and provides a library of recruitment resources. The RIC conducted Community Engagement Studios for message refinement and developed several resources, including an image gallery of patients from diverse racial and ethnic backgrounds, electronic consent (eConsent) tools and best practices, and instructional videos. In addition, RIC translated the tool into Spanish and developed social media campaigns for ResearchMatch.
- **CTSA Institutional Career Development Programs (KL2 and TL1): Frontlines of COVID-19.** Dr. Kurilla informed the Council that KL2 scholars, TL1 trainees and experienced clinical investigators are on the frontlines with COVID-19 research. KL2 scholar Alexander Melamed, M.D., M.P.H., at Columbia University identified an association between socioeconomic condition, environment and COVID-19 status in pregnant women. TL1 trainee Hayley Waterman, at the University of Washington, has been working to refine the next generation of immune approaches to COVID-19 treatment. Supported by a FY 2015 University of Colorado CTSA Community Engagement award focused on the administration of cardiopulmonary resuscitation (CPR) in much needed communities, Comilla Sasson, M.D., M.H.S., Associate Clinical Professor of Emergency Medicine, University of Colorado School of Medicine, subsequently developed a American Heart Association (AHA) National CPR program. As vice president for Emergency

Cardiovascular Care Science and Innovation at the AHA, Dr. Sasson tracked the effect of COVID-19 on CPR training.

- **The Center for Leading Innovation and Collaboration** and CTSA will hold a virtual UnMeeting (i.e., nontraditional meeting) on September 30, 2020, to address clinical research in the COVID era and beyond. Participants will discuss strategies to enable efficient research in the face of the pandemic and how lessons learned can help shape future best practices in translational and clinical research. Participants will consider whether altered practices, such as eConsent and distance monitoring, should continue after the pandemic.

### ***Discussion***

Dr. Kurilla addressed a question posted by a public attendee regarding when the convalescent plasma randomized control trial would report results. Researchers involved with the trial assess the data at intervals, with a definitive assessment likely the end of October 2020. The NYU Continuous Monitoring of Pooled International Trials of Convalescent Plasma for COVID-19 Hospitalized Patients (COMPILE) program is another aspect of the CONTAIN trial that is working in the United States and internationally to accumulate data from convalescent plasma trials. The pooled data will be used to identify the best use of convalescent plasma.

- XI. CURES ACCELERATION NETWORK REVIEW BOARD UPDATE: Ronald J. Bartek, M.A., Co-Founder and Founding President, Friedreich’s Ataxia Research Alliance, and Chair, CAN Review Board; G. Lynn Marks, M.D., Senior Advisor, Tunnell Government Services, and Vice Chair, CAN Review Board**

An update was provided on the Gene Therapy Issue Resolution Program, the Repurposing Off-Patent Drugs Workshops and the CAN Review Board Working Group for Real-World Applications for Mature Programs (RAMP).

### **Gene Therapy Issue Resolution Program**

Mr. Bartek reminded the Council that the Gene Therapy Issue Resolution Program was motivated by the August 20–21, 2018, jointly sponsored NCATS/FDA workshop on gene therapy for rare diseases, in which participants concluded that the existing gene therapy programs were confounded and impeded by six thematic issues, all needing a resolution. In December 2018, the CAN Review Board proposed and approved a series of gene therapy workshops engaging multiple stakeholders to resolve gene therapy issues and widely disseminate solutions. In January 2019, the Council approved the Gene Therapy Program and the CAN Review Board launched a series of six workshops, of which, five have convened and one remain:

- An NCATS “Virtual Workshop on Systemic Immunogenicity Considerations for AAV-mediated Gene Therapy” is scheduled for November 30–December 1, 2020. To date, 900 stakeholders from government, industry, patient advocacy, and academic entities have registered.

A final workshop on the development of actionable funding initiatives is being planned. Industry partners and government agencies have expressed strong interest.

### **Repurposing Off-Patent Drugs Workshop**

Dr. Marks reported on the Repurposing Off-Patent Drugs Workshop series. Discussions began with the May 2019 Council and Board meeting, indicating that CAN Review Board and NCATS are well situated to unite multiple stakeholders to confront the issue of drug repurposing. After discussions on a list of challenges and key questions at the September 2019 Council and Board meeting, the “Repurposing Off-Patent Drugs: Research and Regulatory Challenges” workshop was planned and convened on December 5–6, 2019. Key issues emerged from the workshop series. First, the problems associated with repurposing drugs are not insurmountable, but the current models do not have a unified goal or approach. Second, no single group is responsible for drug repurposing. Third, a consortium approach is needed to catalyze solutions. In addition, workshop breakout groups were asked to prioritize problems surrounding drug repurposing efforts and report ideas for solutions. Several themes emerged, including a need for data prioritization, cost savings use case and systematic resources.

Dr. Marks summarized the next steps and noted that program deliverables have been delayed by the diversion of NCATS resources to the COVID-19 response. A workshop summary for the public is being prepared and will be released in the upcoming months. A drug repurposing toolkit is under development, and meetings with NCATS leadership will be held to examine the CAN Review Board and its authorities, regarding special capabilities to support drug repurposing for rare disease patients.

### **CAN Review Board RAMP Working Group**

Dr. Bartek reminded the Council that the RAMP Working Group, approved by the CAN Review Board in December 2019, is charged to review and assess CAN Review Board and its authorities, prioritize and sunset projects, consider long-term sustainability and identify ways of engaging stakeholders. NCATS envisions enabling a CAN Review Board “superhighway” for implementing translational science. A single project, with an annual budget capped based on the CAN regular appropriations, begins at NCATS, with a destination of the real-world. Advancing a mature CAN Review Board project to real-world application involves many challenges. Advancement can be limited by budget caps, stakeholder involvement and commitment, inadequate mechanisms for project release, and poor communication with potential stakeholders. These challenges can be addressed by raising awareness, strengthening partnerships, engaging stakeholders and developing the skill set needed to make decisions about advancing or discontinuing projects.

Mr. Bartek acknowledged the RAMP Working Group members. To begin its activities, the Working Group will convene 1-hour video meetings, beginning with an orientation session on September 30, 2020. At the October 20, 2020, session will be an overview of the CAN Review Board authorities and NCATS collaboration structure. Presentations about each mature CAN Review Board program will be given to the Working Group at meetings in October and November 2020. The Working Group will meet in December 2020 for an in-depth discussion and next steps. A sub-working group structure will be formed for meetings after December 8, 2020 and work will be coordinated electronically.

Dr. Bartek provided a brief overview of the four mature projects to be reviewed by the Working Group, which includes the Tissue Chips for Drug Screening, Drug Screening with Biofabricated 3D Tissue Models, Translator and PaVe-GT programs.

### ***Discussion***

Joni Rutter, Ph.D., read and answered a question from the public regarding on-ramping mature NCATS projects to the real-world setting (i.e., RAMP) and how success would be measured (e.g., number of projects). Dr. Rutter explained that those criteria had not been decided and noted that RAMP will be

successful if the project is adopted and funded by pharmaceutical companies, biotechnology companies, regulatory entities and/or academic organizations. Mr. Bartek added that one parameter of success will be the first project advancement, which will indicate that the CAN Review Board successfully built the multi-stakeholder consortium and mechanisms required for project adoption and use by the real-world. The first success story also will demonstrate how stakeholders can benefit from consortium participation. Dr. Marks noted it is equally important that the projects continue to succeed after real-world adoption. New mechanisms may be needed to ensure continued project support.

Dr. Marks provided his perspective on how the multi-stakeholder approach could help COVID-19 research. Industry, academia and the government all are coming together in the ACTIV clinical trials. The COVID-19 pandemic is a special circumstance, but it demonstrates what is possible when expertise and motives are aligned to focus on an issue. The broad purview of NCATS, translational science, allows it to connect people from different groups and challenge previous assumptions. The Tissue Chips for Drug Screening program, for example, challenges the assumption that animal models are the best way to detect drug toxicity issues. Newly developed drugs are discarded because animal models indicate toxicity, but safety or toxicity in a rat does not necessarily indicate the same response in humans. Safety, efficacy and toxicity testing in organoids may predict human responses more accurately.

Dr. Austin suggested that the RAMP Working Group generate data on return on investment (ROI). The CAN portion of the NCATS budget is comparatively small, because the outcomes of the CAN program could not be predicted when Congress first allocated funding. The CAN program has fulfilled its initial promise, and Congress might be persuaded to lift funding restrictions with clear demonstration of ROI.

Dr. Rosenblatt commented that NCATS could develop a mechanism to identify intramural and extramural translational projects funded by the NIH, and he suggested that projects that are not prioritized by NCATS may be interesting to industrial or academic partners, and a pathway to releasing those projects could be useful.

Mr. Bartek called attention to the Institute of Medicine Report evaluating the CTSA Program, which determined that NCATS should be helping coordinate translational science efforts across the NIH. Dr. Austin noted the DPI-led trans-NIH preclinical therapeutics group worked with NIH ICs to develop an inventory of COVID-19 projects that might be translationally relevant. This mechanism might be applied more broadly to translational research in other areas.

Dr. Lo seconded the idea of publicizing the ROI for NCATS success stories to encourage replication. He also suggested that NCATS could use online platforms to energize PAGs. Stakeholders could be given free access to information about developing commercial interest in educational enterprises, similar to what the Cystic Fibrosis Foundation has accomplished. NCATS could fund a do-it-yourself course for rare diseases to help parents contact one another to create natural histories or patient registries. Biotechnology and pharmaceutical companies would invest in such activities if they could partner with the private sector and the philanthropic sector.

Drs. Austin and Lo highlighted a report published in 2015 in *Science Translational Medicine* describing a simulated ROI for a portfolio of rare-disease therapeutics, which provided motivation to advance projects to a clinical trial. This striking example of how patients can be helped by the pipeline is a direct result of NCATS data.

Dr. Ramoni noted that the UDN developed a translational research navigation tool to match patients and scientists with similar interests. Dr. Austin noted that NCATS had done something similar with the

NCATS Toolkit RaDaR, which might be used as a foundation for future programs to empower patients and energize stakeholders.

## **XII. SPECIAL DISCUSSION OF COVID-19-RELATED ISSUES: Joni Rutter, Ph.D., Deputy Director, NCATS**

Dr. Rutter reviewed key challenges identified in the discussion held at the May 14, 2020, Advisory Council meeting regarding the cessation of all other research due to SARS-CoV-2, the virus causing COVID-19, noting that many of the issues remain relevant.

- **Safety of Scientists.** The safety of scientists is paramount. The importance of communication in the laboratory as research resumes has become clear. Researchers can share calendars to ensure that schedules are staggered and physical distancing can be maintained. Also, appropriate personal protective equipment should be available.
- **Integrity of the Science.** NCATS has been successful in engaging the CTSAs in SARS-CoV-2 research. The pause in research unrelated to SARS-CoV-2 pause will need to be demarcated when analyzing data later to understand the effects of the pandemic.
- **Non-COVID-19 Research.** Although research on SARS-CoV-2 is urgent, other research priorities also are urgent. Solutions include engaging networks working on other diseases and ensuring that overall research continues to be supported. The NIH is successfully proceeding with this effort, but more contact with other networks is required. The N3C network has been working to engage other groups and ensure that agencies researching questions similar to SARS-CoV-2 research concerns are collaborating.
- **Clinical Trial Considerations and Innovation.** At the time of the May 2020 meeting, more than 1,000 trials related to SARS-CoV-2 had been registered on [clinicaltrials.gov](https://clinicaltrials.gov), many related to hydroxychloroquine. The large number of trials restricted the number of participants available for each trial. Suggestions included considering conditional approvals and telemedicine approaches and emphasizing that people who are ill must continue to be treated ethically while adaptations and education on those adaptations are implemented to ensure robust answers. CTSAs have been critical to keeping work ongoing, without disruption during this time.
- **Implications of NCATS' Work on Economic Recovery.** NCATS responded to the suggestion of addressing economic recovery, particularly given the large public health and educational needs. NCATS OPCE and Education Branch developed educational modules and online courses, which have been well received.

Dr. Rutter commented that although the United States remains in the acute phase of the pandemic, conversations are beginning to include consideration of patients whose symptoms have persisted for many months. COVID-19 will be relevant for the near future, and NCATS' work in understanding it will remain a top priority, but must be balanced with NCATS' other priorities and initiatives. Dr. Rutter requested input on how the Council and Board members have been proceeding with their own work, their key takeaways from the pandemic, their ideas for managing resources and whether they have ideas (inspired by SARS-CoV-2) about opportunities for which NCATS is uniquely suited.

### ***Discussion***

Dr. Austin remarked on the cognitive dissonance caused by the steady or increasing COVID-19 case numbers while the rates of other diseases increase because patients are reluctant to seek treatment during the pandemic. He noted that NCATS has a responsibility to preserve and maintain the health of everyone — not only COVID-19 patients — and requested the Council’s perspectives as stakeholders and taxpayers.

Dr. Stoner commented on the importance of balancing NCATS’ important initiatives with SARS-CoV-2 research, noting that the value of science for human health has been obscured in the public discourse and could be emphasized by NCATS as a component of its public education initiatives. Dr. Rutter agreed about the importance of public health education and acknowledgement that this situation is unusual. She reiterated that prevention and wellness efforts have decreased, so an increase in diagnoses of diseases that could have been identified earlier is likely, and NCATS should raise awareness about this concern.

Dr. Rutter responded to a public comment that NCATS is well placed to contribute to collaborative efforts because of its emphasis on infrastructure, agreeing that N3C has successfully built new infrastructure based on existing ideas. She pointed out that the urgency of the pandemic has prompted increases in the speed and resources needed to improve infrastructure. The changes NCATS has helped implement in response to the pandemic will have long-lasting effects.

:: Rachel Ramoni posted in the Chat to all participants: VA is working extensively on virtual trials and about 40% of VA patients are rural.

:: Audie Atienza posted in the Chat to all participants: CMS is also thinking about telemedicine/telehealth; <https://www.natlawreview.com/article/cms-administrator-verma-calls-permanent-expansion-telehealth-access-after-covid-19>

Dr. Lo inquired about the possibility of continuing some of the disrupted trials through telemedicine. He suggested that researchers consider SARS-CoV-2 as a feature, rather than a nuisance, and use the opportunity to design the next generation of telemedicine-based clinical trials that can reach more people, particularly those who have had difficulty participating in standard trials. He also suggested a workshop on this topic, with NCATS as a pioneer, noting that telemedicine experts would have an incentive to develop new technology and participate in a workshop. Mr. Bartek remarked that such a workshop should include regulatory personnel, such as representatives from the FDA. He further emphasized that some endpoints requiring in-person visits cannot be collected through telemedicine during the pandemic and noted that regulators will need to explore how those lost data will be accommodated. Khaled Bouri, M.D., M.P.H., commented that early engagement with FDA has been successful in past trials, but standards to regulate new technology will need to be developed.

Dr. Austin explained that although some trials have moved to entirely remote measurements, many stakeholders continue to view this shift as a temporary measure, rather than a desirable evolution. He noted the need to better understand the incentives that might drive organizations to return to the in-person model, such as restrictive reimbursement rules, as well as the difficulty of credentialing providers in multiple states. The pandemic likely will spur change in the ecosystem, but stakeholders must collaborate to understand the incentives that affect the homeostasis of this ecosystem and prevent a return to prior restrictions. Dr. Reddy emphasized the importance of collaborating with stakeholders who are invested in advancing scientific progress, rather than those interested in maintaining the status quo.

Dr. Stoner suggested that current adaptations viewed as mitigation efforts in response to the pandemic will require effort to continue as progress toward more inclusive, more thorough trials in the future.

Dr. Rutter pointed out the need to ensure that virtual trials are implemented in a way that reaches minority, rural and other underserved communities, as well as participants who have difficulty traveling to a clinic, such as patients who are disabled or older. Although reaching these communities would be an important step in ensuring that virtual trials are conducted well, many underserved communities do not have access to the technology required for virtual trials and telemedicine. The key takeaway from these discussions is the importance of communicating early and often.

Although many researchers remain concerned that SARS-CoV-2 research will reduce funding for other science, Dr. Holman pointed out that most research has been proceeding well to date under the changed conditions at his institution. Dr. Austin reiterated that both basic research and research on other diseases remain as critical as COVID-19 research for preserving health.

**XIII. ADJOURNMENT OF THE OPEN MEETING**

Dr. Austin thanked all of the participants for their input. He noted that the COVID-19 discussion will continue at the January 14, 2021, Council meeting; new members likely will have been added to the Council and Board by that time. Again, a poll will be sent to the Council and Board to schedule the second day of the meeting to be held either January 13 or January 15. Dr. Austin adjourned the open portion of the meeting on September 18, 2020, at 3:01 p.m. ET.

**CERTIFICATIONS**

We hereby certify that, to the best of our knowledge, the foregoing minutes and supplements are accurate and complete.

\_\_\_\_\_  
Christopher P. Austin, M.D.  
Chair, NCATS Advisory Council;  
and  
Director, National Center for Advancing Translational Sciences, NIH

\_\_\_\_\_  
Date

\_\_\_\_\_  
Anna L. Ramsey-Ewing, Ph.D.  
Executive Secretary, NCATS Advisory Council;  
Executive Secretary, Cures Acceleration Network Review Board;  
and  
Director, Office of Grants Management and Scientific Review, NCATS

\_\_\_\_\_  
Date