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

26th Meeting of the
Advisory Council

Minutes of Virtual Meeting
January 14–15, 2021

The National Center for Advancing Translational Sciences (NCATS) Advisory Council held a meeting in open session on January 14, 2021, from 1:00 p.m. to 3:00 p.m., and on January 15, 2021, from 1:00 p.m. to 4:00 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 January 14, 2021, 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.
Theodore R. Holman, Ph.D.
Andrew W. Lo, Ph.D.
Brad Margus, M.B.A.
Gilbert "Lynn" Marks, M.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
Frank F. Weichold, M.D., Ph.D., (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 January 14, 2021, at 11:56 a.m. ET.

JANUARY 14, 2021

III. CALL TO ORDER, OPEN SESSION DAY 1

Dr. Austin called the meeting to order and welcomed members and guests to the 26th meeting of the NCATS Advisory Council. He noted that the meeting will consist of two sessions: Day 1, January 14, 2021, from 1:00 p.m. to 3:00 p.m. and Day 2, January 15, 2021, from 1:00 p.m. to 4:00 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. APPROVAL OF MINUTES: Anna L. Ramsey-Ewing, Ph.D., Executive Secretary, NCATS Advisory Council and CAN Review Board

Members unanimously approved the minutes from the September 2020 Council meeting.

V. APPROVAL OF 2021 NCATS ADVISORY COUNCIL OPERATING PROCEDURES: Anna L. Ramsey-Ewing, Ph.D., Executive Secretary, NCATS Advisory Council and CAN Review Board

Members unanimously approved the 2021 NCATS Advisory Council Operating Procedures.

VI. CONFIRMATION OF DATES FOR FUTURE MEETINGS: Anna L. Ramsey-Ewing, Ph.D., Executive Secretary, NCATS Advisory Council and CAN Review Board

Anna L. Ramsey-Ewing, Ph.D., explained that the Advisory Council and CAN Board will convene meetings separately beginning in May/June 2021, noting that the meetings likely will be held in tandem because a subset of the members simultaneously serve on both groups. She also noted that the dates and platform of the meetings, virtual or in-person, are to be determined.

Dr. Austin added that this administrative change in meeting structure addresses two issues that have been topics of ongoing discussion in NCATS. First, participation on committees is regarded as one period of service for groups convened under the Federal Advisory Committee Act. Members who serve concurrently on the Council and Board have shorter terms because each appointment is not counted as a period of service in its entirety and turnover is more frequent—which disrupts the ability to review

new projects from concept to outcome. Second, having two appointments for approval simultaneously from the U.S. Department of Health and Human Services (HHS) is unusual, presents challenges in accommodating all parties, and causes delays in roster completion. The new format should resolve these issues. Meetings of the Council and Board, whose missions are slightly different, will continue on an NCATS-established schedule.

Dr. Ramsey-Ewing confirmed the schedule for the meetings of the NCATS Advisory Council and reviewed the tentative schedule of the CAN Review Board for the remainder of 2021 and 2022:

Advisory Council

- May/June 2021 TBD
- September 23, 2021
- January 20, 2022
- May 19, 2022
- September 22, 2022

CAN Review Board

- May/June 2021 TBD
- September 24, 2021
- December 10, 2021
- January 21, 2022
- May 20, 2022
- September 23, 2022
- December 9, 2022

VII. DIRECTOR'S UPDATE: Christopher P. Austin, M.D., Director, NCATS, Chair, NCATS Advisory Council

Dr. Austin began by extending his appreciation to Mr. Ronald J. Bartek, Mr. Brad Margus, and Dr. Gilbert "Lynn" Marks, who recently completed their 4-year terms as members of the Advisory Council and CAN Review Board. He presented a retrospective of NCATS' fiscal year (FY) 2020, "A Look Back at 2020: A Remarkable Year of Collaboration, Innovation and Acceleration." Dr. Austin framed his updates and highlights on progress in some of the NCATS offices, divisions, and programs on this theme, which also is NCATS' new tagline — Collaborate, Innovate and Accelerate — one that emphasizes the Center's core values. He also reported on the NCATS FY 2021 budget.

Dr. Austin reminded participants that NCATS work in FY 2020 was primarily dedicated to addressing the coronavirus disease 2019 (COVID-19) pandemic, noting that new cases, hospitalizations and deaths are at an all-time high, based on the most recent data from the COVID-19 Tracking Project of *The Atlantic*. He pointed out the extent to which those efforts accelerated progress, and demonstrated the importance and potential of translational science across the NIH, other government agencies, and the broader United States.

Collaborate

NCATS took an unprecedented, open collaboration-based approach to addressing the COVID-19 pandemic. Up-to-date information can be accessed from the NCATS COVID-19 webpage — "A Translational Approach to Addressing COVID-19" — launched in May 2020. Dr. Austin highlighted some of those activities and other NCATS collaborations.

- **COVID-19 OpenData Portal.** The Division of Preclinical Innovation (DPI) launched OpenData Portal, an online data resource to share data and information rapidly and publicly on COVID-19-related drug discovery data (e.g., assay development, protocols, and high through-put screening) for all approved drugs. NCATS is sharing its data from 13 SARS-CoV-2 (the novel coronavirus that causes

COVID-19) drug screens in the portal, totaling 500,000 data points. To date, 27,000 visitors have logged into the site. The DPI will expand this resource to include more complex data types (e.g., image-based screens) and integrate related data from external partners in the United States and globally. The Portal has been adopted by the ACTIV (Accelerating COVID-19 Therapeutic Interventions and Vaccines) public–private partnership as the site to display the COVID-19 .

- **SARS-CoV-2 Serosurvey.** In April 2020, NCATS — in collaboration with the National Institute of Allergy and Infectious Diseases (NIAID), National Institute of Biomedical Imaging and Bioengineering, and National Cancer Institute (NCI) — initiated a serosurvey to enroll a cohort of 10,000 healthy volunteers from across the United States who had not had diagnosed COVID-19, in order to determine the rate of asymptomatic infection in the population. NCATS Clinical and Translational Science Award (CTSA) Program Hubs at the University of Alabama at Birmingham and University of Pittsburgh facilitated the study recruitment and representative sampling. A manuscript of the findings has been submitted for publication and longitudinal follow-up studies (funded by the NCI) at 4 and 8 months have begun. In addition, a rare disease patient serosurvey study — through the Rare Diseases Clinical Research Network (RDCRN) — will soon be underway.

- **NCATS' COVID-19 Translational Science Story.** NCATS collaborated with colleagues across the NIH and beyond to develop a video series, host digital events and launch webpages to share the Center's story regarding its translational science approach to the COVID-19 pandemic. This pandemic response approach—not business as usual — is better and cheaper, as well as more rapid, effective, and efficient.

- **Development of Investigational New Drugs for Rare Diseases.** The NCATS Therapeutic Development Branch (TDB) partners with academic institutions, biotechnology companies, and patient advocacy groups to bridge the funding gap (so-called valley of death) from lead compound optimization to preclinical development of promising new drugs. In FY 2020, the TDB progressed 12 projects toward FDA investigational new drug (IND) submissions, including INDs for drugs treating addiction/pain in the Helping to End Addiction Long-term℠ Initiative or NIH HEAL Initiative℠ and COVID-19. Two of the 12 project INDs have cleared FDA approvals for human studies, one investigating Prader-Willi and Hermansky-Pudlak syndromes and a second evaluating Fuchs corneal dystrophy.

- **Toxicology in the 21st Century (Tox 21) Project.** A landmark publication on the Tox 21 10K chemical library appeared in July the *Chemical Research in Toxicology.* NCATS has for the past 15 years has been collaborating with the National Institute of Environmental Health Sciences, U.S. Environmental Protection Agency, and the FDA on the Tox 21 project to identify the biological effects of these 10,000 chemical compounds that are potentially harmful to humans.

- **CTSA Hubs: COVID-19 Pandemic Community Engagement.** The CTSA Hubs, long-standing and trusted community partners, rapidly pivoted their work toward addressing COVID-19 health disparities. The CTSA Hubs are actively working with community partners on initiatives to speed the discovery and delivery of COVID-19 treatments, including vaccines to those in greatest need. Further details can be accessed from the NCATS webpage, "Community Engagement at CTSA Hubs During the COVID-19 Pandemic." In addition, the CTSA Hubs are collaborating with the National Institutes of Health (NIH) on two programs: (1) Community Engagement Alliance (CEAL) Against COVID-19 Disparities and (2) Rapid Acceleration of Diagnostics for Underserved Populations (RADx-UP). Eight of the 11 CEAL research teams are within the CTSA community engagement groups. Six

CTSA Hubs were awarded RADx-UP supplements for projects to improve the accuracy and reach of COVID-19 testing in communities most affected by the pandemic.

- **Workshops and Meetings.** NCATS collaborated on several meetings with other NIH Institutes and Centers. The NCATS Rare Disease Day at NIH was held in February 2020; it was the last in-person meeting before the COVID-19 pandemic. In collaboration with NIAID, NCATS cosponsored the NIH Virtual SARS-CoV-2 Antiviral Therapeutics Summit in November 2020: more than 1,000 attended, and a report is soon to be released. On November 30–December 1, 2020, NCATS convened the virtual "Workshop on Systemic Immunogenicity Considerations for Adeno-Associated Virus (AAV)-mediated Gene Therapy" and hosted the 2-day "Assay Guidance Workshop for High-Throughput Screening and Lead Discovery" November 18–19, 2020.

- **Scientific and Budgetary Planning.** NCATS initiated a Center-wide operations planning process to provide a proactive framework for scientific and budgetary planning activities. The Office of Policy, Communications and Education (OPCE) Policy Branch led by Meredith D. Temple-O'Connor, Ph.D., had extensive engagement in congressional-related activities, including attending members' staff meetings, drafting the annual NCATS Congressional Justification and responding to member and U.S. Government Accountability Office inquiries.

- **Health Disparities Action Plan.** In June 2020, Dr. Austin and the OPCE Education Branch began developing a health disparities action plan as a framework to guide NCATS activities focused on scientific workforce development and address health disparities. Since the last update, NCATS initiated a cross-NCATS Health Disparities Action Plan Working Group being led by Penny W. Burgoon, Ph.D., director, OPCE, to coordinate the activities; as well as an Inclusion, Diversity, Equity in Action (IDEA) Council. A new NIH-wide effort on this topic is soon to be announced, and NCATS staff will be participating.

- **NCATS Virtual Operations.** Dr. Austin reported on NCATS' management of the Center during the COVID-19 pandemic after transitioning to teleworking and shifting its in-person day-to-day operations to a remote platform. NCATS staff have collaborated and stayed connected through weekly and then bimonthly virtual town halls (27 to date), and receiving regular email updates on COVID-19-related activities and NCATS programs. NCATS rapidly shifted from face-to-face meetings and conferences to a virtual platform. More than 8,000 events have been convened, occupying more than 10,000 hours.

Innovate

- **Tissue Chips in 2020.** NCATS issued 10 grants in support of the new Clinical Trials on a Chip initiative. The Tissue Chips in Space program sent five projects to the International Space Station between May and December 2020. Both initiatives are extensions of the NCATS Tissue Chip for Drug Screening program.

- **COVID-19 Tissue Chips.** NCATS-funded investigators at the Wyss Institute for Biologically Inspired Engineering (Harvard University) leveraged their lung-on-a-chip model designed to study influenza to investigate viral entry of SARS-CoV-2. A proof-of-concept study is in progress to identify existing drugs that can be repurposed for pandemic viral applications.

- **Microphysiological Systems (MPS) for COVID-19 Research (MPSCoRe) Working Group.** Dr. Austin called attention to a joint MPSCoRe Working Group to coordinate global MPS efforts to study COVID-19 and future infectious disease applications. The MPSCoRe Working Group is being led by the United Kingdom National Centre for the Replacement Refinement & Reduction of Animals in Research (N3CRs). Partners include the U.S. National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) teams, NCATS, NIAID Division of Microbiology and Infectious Diseases, and U.S. Army Combat Capabilities Development Command Chemical Biological Center. Sixty members have accepted targeted invitations to share data to facilitate application of this platform for COVID-19 and future pandemics. Further details on the Working Group's objectives and activities and overall MPSCoRe effort can be accessed from the N3CRs website.

- **CURE ID.** NCATS Division of Clinical Innovation (DCI) and FDA co-developed CURE ID—launched in December 2019 and updated in May 2020—a mobile app designed to capture data on clinicians' experiences with novel uses of existing drugs (i.e., repurposing) during the COVID-19 pandemic. Notably, 1,109 clinical cases have been reported using the CURE ID app and website, identifying 250 repurposed drugs (e.g., hydroxychloroquine and azithromycin) across 1,327 clinical trials.

- **COVID-19 Testing Small Business Innovation Research (SBIR) Grant.** Dr. Austin was pleased to announce that one NCATS SBIR program awardee, GoDx Inc., successfully completed clinical validation of its rapid, inexpensive Go-COVIDx™ lateral flow assay/test, achieving good performance in patient samples. An additional SBIR grant supported GoDx in filing an FDA Emergency Use Authorization application to manufacture and commercialize the test. The product is now being advanced to the manufacturing phase.

- **NCATS Online Course in Translational Science.** The OPCE Education Branch designed a new online course titled "Principles of Preclinical Translational Science: A Case Study from Cancer Drug Discovery and Development." This course modeled a case-study approach, leveraging the NCATS preclinical project evaluating metarrestin in metastatic tumors, as a first case. Rigorous educational evaluation methods are incorporated, and participants from around the country, across employment sectors and career stages, are attending.

- **NCATS–FDA Translational Science Interagency Fellowship.** Dr. Austin reminded the Council that a joint postdoctoral fellowship and 3-year program, sponsored by the FDA and NCATS Intramural Research Program, aims to provide dual training in preclinical translational science and regulatory science. The deadline for the first round of applications is February 15, 2021.

- **Office of Grants Management and Scientific Review (OGMSR).** Dr. Austin noted the OGMSR infused innovation in funding, peer review, and grants management during the COVID-19 pandemic. The NCATS FY 2020 appropriations needed to be distributed across multiple researchers in the extramural community residing in the United States and internationally. OGMSR staff (1) developed the first NIH "urgent" funding opportunity for new awards, (2) led expedited development and publication of NCATS and key trans-NIH funding opportunities, (3) designed and implemented a toolkit for objective review of COVID-19 applications, (4) compressed the timeframe to review and award grants, and (5) complied with numerous special requirements for reporting and tracking of COVID-19-related activities. In addition, the OGMSR

and NCATS colleagues staffed a booth at the 2020 NIH Virtual Seminar on Program Funding and Grants Administration, sharing information about the NCATS application and review process, with the more than 20,000 attendees.

Accelerate

- **National COVID Cohort Collaborative (N3C).** A collaboration between NCATS Information Technology/Informatics groups, CTSA Hubs, and the Center for Data to Health (CD2H), N3C is accelerating COVID-19 research and improving clinical care. The N3C Data Enclave opened to researchers in September 2020 to share real-world clinical data in a harmonized, centralized and secure manner. Information from more than 2.6 million COVID-19 patients is stored in the Enclave. Eighty-two projects have been approved to access N3C data.

Dr. Austin explained that NCATS and the CTSA Program are playing lead roles in conducting rigorous clinical trials to test potential treatments in hospitalized adults with COVID-19. He provided an update on those trials.

- **Accelerating COVID-19 Therapeutic Interventions and Vaccines Randomized Master Protocol 1 of Immune Modulators (ACTIV-1 IM).** The ACTIV-1 IM launched October 2020 and is evaluating the efficacy and safety of three immunomodulators, targeting different components in the immune pathway. The aim is to reduce the effects of the hyperimmune response in moderately or severely ill hospitalized COVID-19 patients. This trial is funded by Operation Warp Speed and NCATS, has 25 active clinical sites in the United States, and leverages the Trial Innovation Network (TIN) and the CTSA Program.

- **NCATS Convalescent Plasma Randomized Control Trials (RCTs).** Two RCTs led by CTSA Hubs are evaluating blood plasma donated by people who have recovered from COVID-19. One, the Convalescent Plasma to Limit COVID-19 Complications in Hospitalized Patients Trial (commonly called CONTAIN COVID-19) managed by New York University and Albert Einstein University, is active in 17 sites. The second, the Passive Immunity Trial of the Nation for COVID-19 (commonly called PassItOnII) led by Vanderbilt University, is active in 20 sites. NCATS is accelerating translation by establishing a format for direct data submission to the FDA and promoting harmonization of plasma assays. NCATS recently has become involved in a third convalescent plasma RCT, the VA Coronavirus Research and Efficacy Studies (commonly called VA-CURES) study.

Opioid addiction remains an urgent public health crisis. Deaths from drug overdose have almost doubled during the COVID-19 pandemic. NCATS has applied innovative methods, tools, technologies, and platforms (preclinical and clinical) to address the opioid crisis. Dr. Austin provided an update on two NCATS projects that address opioid addiction.

- **NIH HEAL Initiative[SM].** The DPI is overseeing 51 ongoing NIH HEAL Initiative projects that address preclinical research in pain and opioid use disorders. The HEAL Initiative Pain Management Effectiveness Research Network (Pain-ERN), managed by the CTSAs, has the goal of testing interventions for effectiveness in treating pain. Six Pain-ERN trials are using the NCATS TIN infrastructure, one the NCI Community Oncology Research Program, and one the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) Maternal

Fetal Medicine Units. Pain types being studied include osteoarthritis and post-cancer therapy, chronic pain co-occurring with opioid use disorder, and acute post-surgical pain.

- **A Specialized Platform for Innovative Research Exploration (ASPIRE).** Dr. Austin reminded participants that the goal of ASPIRE is to spur innovation and catalytic approaches to solve the opioid crisis by developing an integrated system of novel chemistries, data-mining and analysis tools and technologies, and biological assays. Submissions are being accepted until February 28, 2021, for the Stage 2 ASPIRE NIH HEAL Initiative Challenge, Reduction-to-Practice.

FY 2021 Budget

Dr. Austin reported that the FY 2021 budget (Consolidated Appropriations Act 2021) was enacted on December 27, 2020; it contains all 12 annual appropriations and includes a fifth COVID-19 supplemental funding. In addition to the regular appropriations, NCATS was allotted $10 million to create a Consortium for Innovation in Large-Scale Gene Vector Production. Dr. Austin emphasized that this initiative is intended to enable gene therapy translation to patients, regardless of the disease. He noted that this effort aligns with the work of the CAN Review Board.

VIII. PROGRAM UPDATE: OFFICE OF RARE DISEASES RESEARCH: Anne R. Pariser, M.D., Director, Office of Rare Diseases Research (ORDR), NCATS

Anne R. Pariser, M.D., provided updates on the activities and ongoing programs in the ORDR. She acknowledged the ORDR team and announced two new staff members: Linda Ho, M.P.P., presidential management fellow, and Yanji Xu, Ph.D., program director for informatics. Dr. Pariser reminded the Council of the ORDR mission: advancing rare diseases research to benefit patients. ORDR staff facilitates coordination among multiple stakeholders in the rare diseases community. The underlying problem — a public health problem — the ORDR is trying to solve is that approximately 7,000 known rare diseases are affecting 1 in 10 people in the United States, translating to 25 to 30 million people, of whom the majority are predominately in the younger population. Although the molecular basis for most of the 7,000 rare diseases is known, only 600 have established therapies. To address its mission, the ORDR directs programs in three areas: data and informatics, research, and collaboration.

Dr. Pariser framed the updates, as did Dr. Austin, within the themes that align with NCATS core values: Collaborate, Innovate and Accelerate. She began with innovative programs and strategies.

Innovate

- **Platform Vector Gene Therapy (PaVe-GT).** A research pilot through which four gene therapies for rare monogenic disorders are being developed simultaneously, PaVe-GT is using a platform design and AAV gene therapy vector. Multiple therapies for the same disease can thus be tested in the same clinical trial, a paradigm shift from a traditional one-at-a-time trial design. PaVe-GT, also a master protocol and umbrella trial, is in its early stages of startup. The ORDR and the PaVe-GT team reported on the status of the trial in the October 2020 issue of *Human Gene Therapy*. PaVe-GT is a collaboration among the National Human Genome Research Institute, National Institute of Neurological Disorders and Stroke (NINDS), and three NCATS offices — ORDR, TDB, and the Office of Strategic Alliances (OSA).

- **Diagnostic Odyssey.** Another strategy for studying more rare diseases in more patients focuses on improving the diagnostic process, leading to more diagnoses of rare diseases. Many people with rare diseases go undiagnosed, and the path to a diagnosis can be long and difficult. To address the challenge of diagnosing rare disease patients, the ORDR had published a now-closed funding opportunity announcement (FOA) to support multidisciplinary approaches to diagnoses combining machine assistance, early genomic analysis, and clinical consultation.

- **Shared Molecular Etiologies.** Many phenotypes for many rare diseases exist, but far fewer genetic etiologies that underlie rare diseases are known. By focusing on shared genetic etiologies, rather than individual phenotypes, investigators can create larger treatment pools and gain efficiencies in therapeutic development. Using this innovative strategy, patients with different diseases that are caused by the same underlying genetic abnormality can be treated with the same therapy. The ORDR has published two FOAs encouraging studies focusing on the treatment of shared molecular etiologies in non-oncology diseases.

- **RDCRN.** Established in 2003 through the Rare Diseases Act, the RDCRN comprises 20 consortia and 1 Data Management and Coordinating Center (DMCC) that are focusing on clinical trial readiness while studying approximately 250 rare diseases. The fourth award cycle (RDCRN4) cohort started in FY 2019, and the priorities have been clinical trial readiness. Within the RDCRN is a Research Commons, with the goal to scale to many consortia, establishing a research community workspace. The Commons provides unifying principals for the consortia and DMCC and manages services through an NCATS-hosted cloud. The DMCC and NCATS have established an RDCRN Tool Garden, a suite of software and tools developed in response to researchers' needs.

- **COVID-19 Patient Impact Survey.** Rare disease patients have been disproportionately affected by the COVID-19 pandemic, during which they have had difficulty accessing health care services. The RDCRN developed the COVID-19 Patient Impact Survey to establish the nature and degree of this impact. A total of 4,129 surveys from 50 states, Puerto Rico and the District of Columbia have been collected, including responses from patients representing more than 200 rare diseases. This survey is now closed and undergoing analysis.

Accelerate

- **Genetics and Rare Diseases (GARD) Information Center.** The GARD Information Center, an online health information website established in 2003 that contains 6,500 disease pages, fields approximately 900 inquiries per month and provides individualized support for people affected by rare diseases. GARD 2.0 is a 2-year effort to modernize this disease information by making machine-assisted tools that will enhance information accuracy, identification, sharing, and reusability to optimize patient knowledge and accessibility. Using machine-assisted approaches and innovative data management systems, investigators have developed cutting-edge tools to better organize the available data. For example, using a knowledge-graph database, the DPI informatics team established connections and relationships among diseases to better organize and use the data on these diseases. Such organizational systems facilitate the seamless application of knowledge about one disease to another. This organizational model has been launched and moved to the NCATS cloud.

- **NCATS Toolkit for Patient-Focused Therapy Development.** Dr. Pariser noted that the NCATS toolkit was launched in 2017, with the intent of being a one-stop-shop of online resources for patients. Efforts are in progress to expand the content and make the toolkit more patient-friendly.

Collaborate

- **NCATS RDD.** Since 2009, the ORDR has organized the NIH RDD, an event that highlights NIH-supported rare diseases research, in parallel with the International RDD. This event features presentations by luminaries and researchers; panel discussions; and Technology, Entertainment, Design (TED)-style talks from patients sharing their stories. The 2021 RDD will be virtual and is scheduled for March 1.

- **Rare Diseases Are Not Rare! Challenge 2.0.** NCATS completed the Rare Diseases Are Not Rare! Challenge 2.0, an effort that raises awareness about rare diseases using such media as art, poetry, social media and music. A spoken-word poetry submission — "Keep on Fighting," by Jacob Thompson — was the challenge winner.

- **Gene Therapy Meeting Series.** The ORDR and the CAN Review Board collaborated to convene meetings focusing on gene therapy, which is a programt the Board recommended to NCATS. Four joint NCATS–FDA meetings were hosted during the past 2 years, all of which were very successful and boasted impressive attendance and participation.

- **Impact of Rare Diseases on Patients and Healthcare Systems (IDeaS).** The IDeaS study (previously the Novel Explorations in Rare Diseases) is intended to explore and develop methodologies that will permit objective quantification of direct medical costs in 14 representative rare diseases; document the diagnostic journey of patients with rare diseases; and explore the costs of being un- or misdiagnosed. This effort represents a significant collaboration among NCATS and academic medical centers, insurers and data analytics companies. The first paper for this study is in development and should be disseminated soon.

Looking Forward for 2021

Dr. Pariser highlighted priority areas for the ORDR in 2021, which broadly include improving diagnoses, accelerating research, and making best use of the data.

Discussion

Mr. Margus commented on the rapid speed at which research progressed during the COVID-19 pandemic and suggested that lessons learned from that process could inform the development of new, faster processes by which other diseases (e.g., ataxia telangiectasia [A-T]) could be researched. Dr. Austin agreed, noting that temporary conditions put in place in response to the COVID-19 pandemic — such as exemptions to regulatory or NIH policies, unsustainable overwork, telemedicine, and increased funding — enabled abnormal expediency. Dr. Austin presented the following concept: Because such expediency is now known to be possible, and given a strong sense of urgency and care for the lives of those who could be affected by COVID-19, should that same expediency be applied to other, rarer diseases and does this question become a moral one? He stated that Congress now understands the amount and caliber of work the NIH system can deliver, but maintaining that same quality and output would require changes in policy and funding. To achieve the same progress, speed, and quality of work, investigators need to speak with a unified message.

Mr. Bartek asked how investigators could build a sense of urgency, acquire phenomenal resources, and foster international collaboration in the same way for all rare diseases as was accomplished during the COVID-19 pandemic. Dr. Austin responded that the IDeaS system, specifically, can help others appreciate the scale and expense of the problem at hand. If NCATS can make others realize how expensive rare-diseases health care is to the public, then NCATS can make financially based appeals for change and support by suggesting that making health care more efficient in these spheres can lower overall costs.

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

Dr. Austin adjourned Day 1 of the meeting at 3:08 p.m. ET.

JANUARY 15, 2021

X. 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 26th meeting of the NCATS Advisory Council. He reminded attendees that the open session is being webcast and reviewed the agenda.

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; Gilbert "Lynn" Marks, M.D., Senior Advisor, Tunnell Government Services, and Vice Chair, CAN Review Board; P.J. Brooks, Ph.D., Program Officer, ORDR, NCATS

An update was provided on the Drug Repurposing Project, Gene Therapy Project, and the CAN Review Board Real-World Applications for Mature Programs (RAMP) Working Group.

Drug Repurposing Project

Dr. Marks provided an update on the Drug Repurposing Project, noting the activities prior to and succeeding the NCATS–FDA December 2019 workshop, "Repurposing Off-Patent Drugs: Research and Regulatory Challenges." He elaborated on three problems workshop participants outlined that a drug repurposing project would help to resolve: (1) need for data prioritization, (2) need for a cost-savings use case to demonstrate an incentive for payor participation (e.g., VA health care system), and (3) lack of systematic resources contained in a common location.

:: Rachel Ramoni posted in the Chat to all participants: We do indeed have a cost-savings use case. We need to set up a series of meetings to move this forward.

:: Christopher Austin posted in the Chat to all participants: Many thanks to Rachel for her leadership at VA to helping us develop this use case; her staff have been fantastic!

Dr. Marks announced that in the June 2020 issue of *Driving Insights in Action* Global Forum article, "Repurposing Challenges: Conceptualization of a Research Agenda," Dr. Austin reported details of the repurposing workshop and highlighted its major themes. The workshop Day I videocast and a written transcript can be accessed from the NIH website. The next steps, preparing and publishing a written report of the workshop, developing a drug repurposing toolkit and examining the CAN Review Board and its authorities, have been delayed by the diversion of NCATS staff and resources to the COVID-19 response.

Gene Therapy Project

Mr. Bartek explained that in January 2019 the Council approved the Gene Therapy Project and that the CAN Review Board, in collaboration with NCATS, launched a series of six workshops/conferences addressing six thematic gene therapy issues. All workshops have convened, concluding with the final one that focused on comprehensive immunogenicity issues. No additional workshops on this topic are planned, but the CAN Review Board is open to suggestions.

P. J. Brooks, Ph.D., summarized issues raised and lessons learned at the NCATS 2020 virtual "Workshop on Systemic Immunogenicity Considerations for AAV-Mediated Gene Therapy." He explained that the immune response to AAV vectors is complex and includes the innate immune system, involving non-specific responses to viruses and pathogens and the adaptive immune system that includes responses to antibody production. An additional factor is activation of the complement pathway. Dr. Brooks explained that many first-in-human gene therapies require drug dose escalation, with the lowest dose being the least effective. An immune response to AAV-mediated gene therapy would limit or curtail re-dosing a patient. In addressing this issue, significant progress has been made in recent years in identifying drugs that affect the mechanistic target of the rapamycin pathway and different aspects of the innate immune system that can modulate the immune response to AAV-mediated gene therapy. NCATS' role will be to facilitate data sharing, optimize clinical trial design (e.g., PaVe-GT), and disseminate best practices. In addition, the immunogenicity workshop participants identified issues in AAV manufacturing, including meeting the ongoing market response, needing broad adoption of intellectual property-free manufacturing method, and reducing the amount of empty vector.

CAN Review Board RAMP Working Group

Mr. Bartek provided updates on the CAN Review Board RAMP Working Group and acknowledged the Working Group members and their diverse expertise. The Working Group is charged with making recommendations to enable NCATS to better leverage the power and authorities of the CAN Review Board to transition translational science projects toward real-world utilization in vehicles that are independent of NCATS support. The first order of business is to provide input on transitioning the current four programs — Tissue Chip for Drug Screening, Drug Screening with Biofabricated 3-D Tissue Models, Biomedical Data Translator, and PaVe-GT — and make recommendations on general principles that inform the design, selection, and prioritization of new projects. The Working Group began its activities with a series of orientation sessions from September to November 2020, followed by approach-building sessions commencing December 2020 and to culminate in spring 2021. The preliminary selection criteria for prioritizing new projects has been developed. The final outcome will be formal recommendations to the CAN Review Board.

Discussion

Regarding the economic incentive for repurposed drugs, Andrew W. Lo, Ph.D., called attention to the key issue of whether the FDA would be willing to update the *Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations* (Orange Book) to reflect new patents on generic medications for different purposes. If it is not changed, physicians can prescribe generics off-label, thus preempting incentives. Dr. Brooks noted the ongoing work with the FDA Center for Biologics Evaluation and Research, including one effort involving FNIH to streamline the regulatory process for AAV vectors, but could not speak specifically about potential changes to the Orange Book. Frank F. Weichold, M.D., Ph.D., clarified that changes to the Orange Book would consist of information on the use, risk factors, and adverse events of the drug. FDA is not authorized to direct physicians to use a patented drug versus a similar generic version.

::Rachel Ramoni posted in the Chat to all participants: We could use help in getting connected to a good health economist, as ours are over-subscribed.

Dr. Lo remarked on efforts in the private sector (e.g., Ally Therapeutics, Inc.) focusing on reducing the immunogenicity of AAV vectors and questioned whether NCATS' work complements or competes with that of others. Dr. Brooks acknowledged other work in the field that seeks to engineer improved AAV vectors and noted that some projects are supported by NIH grants. The immunogenicity workshop participants noted new methods under development in the private sector (e.g., Spark Therapeutics, Inc.). NCATS is seeking to collaborate (not compete) with potential partners to identify the best approaches.

:: Christopher Austin posted in the Chat to all participants: To further answer Mike Rosenblatt's question about whether NCATS has programs in medchem modification of currently approved drugs: NCATS has a robust program to do this in our Division of Preclinical Innovation. And NCATS has made the data on all approved drugs screened across over 200 different assays completely public (pos and neg data) so medchemists in the public and private sectors can carry out their own modifications. We always try to remember the famous Sir James Black quote that "The most fruitful basis for the discovery of a new drug is to start with an old drug."

Michael Rosenblatt, M.D., commented that the current gene therapy approaches are first-generation technologies and emphasized the need to be cognizant of the advent of second-generation technologies

likely in the next 5 to 10 years. He asked whether the goal is to exclusively repurpose off-shelf drugs for new uses similar to what had been the case with antivirals and AIDS in the 1980s. Dr. Marks responded that the main focus is on new indications for approved generic drugs. Christine M. Colvis, Ph.D., added that the NCATS repurposing workshop was convened to address off-patent or generic drugs. Incentivizing new indications for an existing drug and changing the label after the initial investments remains an issue, suggesting a need for different cost level and new business model for payors. Dr. Austin emphasized that all potential stakeholders — including scientists, clinicians, payors, intellectual property (IP) representatives, and policymakers — attended the repurposing workshop and came to consensus that enforcing a specific patent to be prescribed would not gain traction in the clinical community.

In response to a question from Dr. Austin regarding when the CAN Review Board RAMP Working Group would complete its work, Mr. Bartek clarified that its timeline is to present formal recommendations in early spring 2021. He noted that subgroups assigned to address the four projects have already begun reporting their recommendations to the full Working Group to facilitate drafting a final comprehensive report.

XII. PROGRAM UPDATE: OFFICE OF STRATEGIC ALLIANCES: Lili M. Portilla, M.P.A., Director, Office of Strategic Alliances (OSA), NCATS

Lili M. Portilla, M.P.A., updated the Council and other attendees on the structure of the OSA. Key to OSA's success is team members who exemplify the characteristics of being team-oriented, having an entrepreneurial attitude, pressing beyond the established policy, and engaging with scientific and program staff. In addition, the OSA provides services to the science team, understands the difference between traditional technology transfer versus strategic alliances, and seeks ways to obtain an affirmative answer. Ms. Portilla explained that OSA's workload increased during the COVID-19 pandemic. The total executed agreements by OSA staff increased by 80 percent and cooperative research agreements (CRADAs) by 7 percent in FY 2020 compared with the previous year. This increase is credited to COVID-19-related agreements, particularly the N3C Data Enclave data transfer agreements.

Ms. Portilla aligned her updates with the NCATS core values of Collaborate, Innovate and Accelerate.

Collaborate

- **Implementation Strategies.** Ms. Portilla noted the critical need to understand the overall strategy and goals of the project. A staged agreement process that addresses the immediate needs of the parties is used. Template agreements can work if custom agreements are not required. Regarding negotiation timelines, agreement arbitrations and scientific project plan development should run in parallel.

- **Research Team Collaborations.** Because of the volume of OSA agreements received in any year, the office has developed an extensive checklist to guide collaborations between research teams. This request system models the airline industry's pre-flight checklist in terms of addressing all the requirements for comprehensive agreements, extending from the project goals and outcome to intellectual property and data management to NCATS' use of the contracts during the project.

Regarding activity statistics in comparison with the other 26 NIH Institutes and Centers (ICs), Ms. Portilla reported that for FY 2020, NCATS ranked third in new employee invention report submissions (28), fifth in new patent fillings (46) and granted domestic/foreign patents (24), and fourth in active CRADAs (22). NCATS OSA achieved this level of success with a budget four to five times smaller than those of the major ICs. The OSA will expand beyond a standard technology transfer model of metrics to one that measures scientific output, public health impact, and economic impact of the office's facilitation of NCATS collaboration. An "OSA Metrics Virtual Workshop" soon will be announced.

- **NCATS Pilot Training Program – Advancing Innovation by Mentoring (AIM).** NCATS, in collaboration with the NCI, launched the AIM program during the COVID-19 pandemic to identify opportunities where research can make the greatest scientific impact. AIM focuses on intramural staff and is designed to build a skill set for evaluating technology that can be applied to future research projects. The goal is to expand the professional network of collaborators, potential licensees, and key opinion leaders to engage with a wider network of scientific experts. Modeled after the NSF Innovation Corps (I-Corps™) program, AIM uses a customer-discovery business model, and teams (lead/principal investigator, trainee, and technology transfer manager) participate in a 4.5-week course. When surveyed, 75 percent of the AIM pilot cohort responded that the course changed their approach to conducting research.

Innovate

Ms. Portilla reviewed the inventions filed by NCATS from FY 2008 to 2020. She highlighted that 80 percent of the NCATS patent portfolio are patents co-owned — with either an NIH IC or a party outside NIH (e.g., a university or company). This ratio is the opposite of other NIH ICs and speaks to the collaborative nature of the DPI, which at any time, has more than 150 collaborations. OSA consolidates the IP rights and provides the partners the ability to manage their patents and take the lead in licensing.

- **Cooperative-Research Collaboration Agreement (C-RCA).** The OSA developed a new simplified agreement to assist collaborators in procurement and licensing joint inventions developed in NCATS. The first of its kind in terms of NIH mechanisms, the C-RCA aims to alleviate unnecessary delays in posting in the *Federal Register* when jointly developed IP is licensed under an existing Inter-Institutional Agreement to the collaborator. The C-RCA has been adopted as part of the NIH Agreement Toolbox.

Accelerate

- **N3C Data Enclave Agreements.** Ms. Portilla explained that the OSA was tasked with developing the *de novo* agreements for the N3C Data Enclave rapidly during the COVID-19 pandemic, without a template. One agreement was needed to address all data levels. The OSA solicited and received input from experts across NCATS and NIH on a suitable model, thus illustrating a team approach to creating agreements. To date, the OSA has executed 250 agreements in support of the N3C Data Enclave, with a turnaround time of 24 to 48 hours. Other NIH ICs have expressed interest in using these model agreements.

- **NCATS Patent Book.** NCATS had a record period of patent issuances between October 2018 and March 2020, particularly in the DPI. OSA developed an NCATS Patent Book, "Innovation at NCATS," to showcase DPI staff and collaborators' efforts in innovation. This commemorative book will be used to market unlicensed technologies and is posted to the NCATS website.

OSA Next Steps

Ms. Portilla noted some next steps for the OSA, including evaluating the office's impact on translating technologies and scientific advances, experimenting with new ways to advertise NCATS collaborations and technologies, evaluating the impact of the AIM Program, and hosting an NCATS technology showcase and a pitch-coaching session.

Discussion

Dr. Weichold lauded NCATS and the OSA for their work, level of creativity, and approach to technology development and commercialization, particularly in the context of the federal government.

Dr. Lo echoed Dr. Weichold's comments and asked about the plans for the NCATS patents, whether investors were being sought, and how the private-sector can partner with NCATS. Ms. Portilla replied that the intent is to use the patents to develop a therapeutic or an intervention for patients, leveraging the licensing success of NCATS inventions. Advancing NCATS' 41 solely owned patents goes against the NIH licensing policy. Dr. Lo noted that firms in the private sector, such as Deerfield Management Company, are partnering with universities to fund translational research, advance patents, and build new companies, and he suggested this as a model NCATS could explore. Ms. Portilla added that discussions are in progress with organizations similar to Deerfield and it is a model the government favors.

Theodore R. Holman, Ph.D., shared his experience in having two NCATS patents, which led to starting new companies. He emphasized that progress requires investments in the discoveries and inquired about ways to improve this process. Ms. Portilla pointed out that OSA interacts with institutions on those projects with patents seeking investors and assists with making introductions to interested parties.

Dr. Holman encouraged the writing of case studies to highlight successful NCATS collaborations; Ms. Portilla agreed to follow up on this idea.

XIII. CLEARANCE OF CONCEPTS

The Council received presentations on three new initiatives and one renewal initiative 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.

Helping to End Addiction Long-term℠ Initiative or NIH HEAL Initiative℠ Translational Science Training: Christine M. Colvis, Ph.D., Director, Drug Development Partnership Programs, NCATS; Steven T. Pittenger, Ph.D., Program Officer, Drug Development Partnership Programs, NCATS

Dr. Colvis presented the NIH HEAL Initiative℠ translational science training concept. The NIH HEAL Initiative, a trans-NIH effort to speed scientific solutions to stem the national opioid public health crisis with a focus on developing novel pharmacotherapies to treat pain, opioid use disorder and overdose. It is well known that therapeutic discovery, development, and deployment is a complex process. Traditional training often occurs within a small segment of this process. In addition, workplace diversity in biomedical research is less than optimal, particularly within therapeutic discovery and development.

The objective of this concept is to provide NIH HEAL Initiative funds to support early- and mid-career scientists who are expert in pain or opioid use disorders research to receive in-depth training in therapeutic development in an academic or government translational research center or in an industry setting. The area of emphasis directly addresses the lack of workplace diversity in drug development by specifically providing translational training to individuals from underrepresented groups. The goal is to build a workforce of investigators better equipped to translate scientific discoveries into clinical breakthroughs.

The NCATS anticipates that this opportunity will provide the fields of pain, dependency, and overdose with scientists better equipped to design experiments with an emphasis on translating discoveries to affect health. Importantly, incorporating a translational perspective in the early- and mid-career stages will promote the guiding NCATS principle of bringing "more treatments to more patients more quickly."

Discussion

Mr. Margus expressed his support for the concept, which is addressing a knowledge gap in drug discovery and development. He commended NCATS for establishing this program focusing on pain research and engaging industry. Mr. Margus encouraged exposing trainees to innovative methods of drug discovery and considering contract research organizations in the training process.

Mr. Bartek, also supportive of the concept, asked whether the training program was restricted to developing treatments exclusive of clinical applications of those treatments. Dr. Colvis explained that the training could be clinically based, but with a clear understanding of the preclinical requirements to arrive at the clinical application. The preclinical trainees also will receive instruction on advancing a therapy to the clinical setting, with an understanding of developing endpoints and identifying a patient population for a study. Dr. Colvis clarified that this translational science training program does not extend to clinical care.

Kiran Reddy, M.D., suggested incorporating regulatory training, which would build the trainees' portfolio, positioning them for opportunities in the biotechnology industry.

Members approved the HEAL translational science training concept with 4 ayes, zero nays, and 1 abstention.

Technological Development and Validation of Remote Measures for Use in Clinical Trials in Individuals with Rare Diseases: Tiina K. Urv, Ph.D., Program Director, Office of Rare Diseases Research, NCATS; Lili M. Portilla, M.P.A., Director, Office of Strategic Alliances, NCATS

Tiina K. Urv, Ph.D., and Lili Portilla, M.P.A., presented an SBIR contract concept on technological development and validation of remote measures for use in clinical trials in individuals with rare diseases. Rare disease patients face significant barriers to participation in clinical trials due to travel limitations, health issues, as well as financial difficulties. Although virtual clinical trials (e.g., remote or decentralized trials) leverage technologies to overcome these barriers, validated measures specific for use in remote clinical trials and studies are missing. This concept proposes to use U.S. small businesses to develop and validate sensitive and specific outcome measures that are technologically viable for use in clinical trials in patients with rare diseases.

The objectives are two-fold: (1) facilitate virtual studies by developing and validating outcome measures that can be assessed remotely and that are suitable for use in clinical trials and (2) develop robust, user-

friendly technologies to collect these assessments. This research will capture accurate and replicable data remotely in the patient's family environment (e.g., adaptive life skills, strength). It also will collect continuous variables and provide a more accurate assessment of the patient's real condition through new measurements made possible by technology.

Consistent with NCATS mission, this concept supports the three "Ds" to develop, demonstrate and disseminate innovative interventions that benefit public health, enabling a more diverse group of individuals to participate in rare disease clinical trials. Because of the success of NCATS SBIR-funded projects in stimulating technological innovation and meeting research and development needs, commercialization of these technologies is expected to result in significant patient benefit.

Discussion

After expressing his support for the concept, Mr. Bartek commented on the value of this approach as a way of using technological advances to obtain additional evidence of a patient's daily ability to perform in his or her home environment, information that often is requested by regulators (e.g., FDA and American Medical Association). He continued that this concept, which is emulating a virtual clinical trial, is capturing needed outcome measures.

Mr. Margus stated that approximately 400 children diagnosed with A-T are disparately located around the United States and thus must travel to nonlocal clinical sites for treatment. He expressed his support for the concept — a remote system that can measure and evaluate rare disease patients — which is applicable to natural history studies. Mr. Margus encouraged having incentives in place to support tool validation of promising techniques (e.g., machine learning–based speech analysis) and creating tools that can be scaled and rapidly implemented.

Rachel Ramoni, D.M.D., Sc.D., remarked on the potential for this concept to provide the framework for a larger effort involving a technology development pipeline for rare diseases clinical trials. Mr. Bartek commented on the need to address the large data sets that are likely to be generated.

Dr. Weichold noted that FDA's interest in this concept is significant, particularly in the context of using real-world evidence for regulation, validating relevant biomarkers for accelerating product development, and enhancing safety for mobile devices. He called attention to two key efforts at the FDA on this topic: the Center for Devices and Radiological Health–led initiative focusing on validating software data packages as a device and another effort that emphasizes standardization and interoperability of data.

In addition to regulatory approvals, Dr. Rosenblatt highlighted two other groups to engage regarding advancing commercial products, including insurance companies (payors) and patients (input on the device).

Members unanimously approved the remote measures for use in clinical trials in individuals with rare diseases concept.

CTSA Consortium-Wide Centers: Resources for Rapid Demonstration and Dissemination (C3-R2D2): Audie A. Atienza, Ph.D., Program Director, DCI, NCATS

Audie A. Atienza, Ph.D., presented a concept on establishing the CTSA Consortium-Wide Centers: Resources for Rapid Demonstration and Dissemination (C3-R2D2) initiative, which proposes to leverage

capabilities and expertise across the CTSA Program to advance Clinical and Translational Science (CTS). Innovations within CTS require multidisciplinary teams with diverse and unique skill sets. Three centers currently share capabilities and expertise across the consortium: the CTSA Data to Demonstrate Health (CD2H), Centers supported through the Trial Innovation Network (TIN), and the Center for Leading Innovation and Collaboration (CLIC).

Over the past few years, CTSAs' successes have expanded beyond coordinating communications, facilitating data harmonization and data sharing, and using innovative approaches in clinical trial recruitment. NCATS proposes the C3-R2D2 initiative to build on these successes and focus on research demonstration and dissemination at the consortium level. The administrative tasks for the CTSA Program are in the process of being transferred to a support contract mechanism approved by NCATS Council during the January 2020 meeting.

The objective of this concept will be to leverage subject matter expertise across the CTSA Program to develop and provide consortium-level resources and capabilities for specific categories of innovative approaches. Potential areas of emphasis may include health information technology (e.g., mobile health/telemedicine, electronic health records interoperability and data exchange), research-impact quantification, trial designs and recruitment approaches, and platforms/processes that facilitate satisfying regulatory requirements. This initiative also will be responsive to emerging high-priority topics.

In establishing the C3-R2D2 initiative, NCATS anticipates overcoming clinical and translational science roadblocks; accelerating dissemination methodologies across the CTSA consortium for uptake of knowledge, research tools, methods, and data; and identifying, implementing, and disseminating consortium-wide resources for faster adoption to positively affect patients and public health. The overarching goal is to rapidly accelerate CTSA consortium-wide collaborations toward innovative, game-changing, high-impact clinical and translational science advances.

Discussion

Emphasizing the challenge in translating discoveries into clinical applications across institutions in a timely manner, Dr. Holman expressed his strong support for this initiative, which plans to establish central dissemination of the next generation of CTSA Program capabilities and resources. He sought clarity about the potential evaluation metrics for success across the 60 CTSA Hubs. Dr. Atienza clarified that common metrics for evaluating programs across the CTSA Program are already in place. Erica K. Rosemond, Ph.D., deputy director, CTSA Program, explained that evaluation metrics on the research resources and those validations will be incorporated in the FOA. Michael G. Kurilla, M.D., Ph.D., director, DCI, and director, CTSA Program, noted that the goal is to explore innovative ways to disseminate information and best practices more efficiently. Over time, metrics from translational science lessons learned across the NCATS programs will be built into the Center's consortium-wide efforts.

Dr. Lo expressed his enthusiasm and support for this concept and suggested using videos posted to the NCATS YouTube channel or strictly educational platforms (e.g., edX.org) as a method of dissemination across NCATS-funded initiatives and programs. Grantees, in a 15- to 20-minute video, could summarize their key findings as an educational component of their project and as a grant deliverable. A digital learning office or similar group then could create thematic programs or courses. Dr. Rosemond pointed

out that the NCATS CLIC is developing stories of impact from across the CTSA Program, which the OPCE Educational Branch could further expand.

:: Penny Burgoon posted in the Chat to all participants: This would be a great translational challenge to consider.

:: Andrew Lo posted in the Chat to all participants: Teaching health care finance online: https://youtu.be/hmGV_c-kriU. Home studio setup: https://youtu.be/jaFHhQktJiw.

In response to a question from Dr. Rosenblatt on the interface of the proposed translational science training program and the C3-R2D2 concept, Dr. Atienza explained that the translational science training program is specific to the NIH HEAL Initiative and is a trans-NIH effort.

Dr. Ramsey-Ewing read a question from an attendee, Martin S. Zand, M.D., Ph.D., regarding whether the current programs—CD2H, CLIC, Recruitment Innovation Center (RIC), and TIN—will be discontinued. Dr. Kurilla replied that the intent is to create an overarching concept that can function as an umbrella for and expand those programs, while capturing emerging technologies.

Members unanimously approved the CTSA C3-R2D2 concept.

Clinical Trial Readiness (CTR) for Rare Diseases: Alice Chen Grady, M.D., Program Officer, Office of Rare Diseases Research, NCATS

Alice Chen Grady, M.D., presented a renewal concept for the CTR for Rare Diseases, Disorders and Syndromes grants program, aiming to support studies that are addressing critical gaps in rare diseases clinical trials, including lack of (1) validated biomarkers and clinical outcome assessments necessary for selecting appropriate endpoints in rare diseases and (2) a trial readiness priority area needed by regulatory agencies.

NCATS proposes this renewal concept to support projects focused on efficiently and effectively advancing candidate rare diseases therapeutics (or diagnostics) into clinical trials and to increase their likelihood of success in upcoming clinical trials. The program focuses on rare diseases that currently (or soon will have) candidate therapeutics or diagnostics ready for testing in clinical trials and projects that leverage partnerships and existing NCATS resources (e.g., RDCRN).

The first CTR grants were awarded in summer of FY 2019. To date, NCATS and the NICHD have collaborated to fund two Small Research Grant (R03) awards and 16 Exploratory/Developmental Research Grant (R21) awards, through three funding cycles. Regarding accomplishments, nine publications citing this relatively young CTR program have been reported in the NIH Research Portfolio Online Reporting Tools, and several projects show promising data. For example, Children's Hospital of Philadelphia investigators are working to validate an objective outcome measure of therapeutic response in a pediatric rare disease population.

NCATS and the NICHD recognize an ongoing need to provide FOAs for studies that address specific gaps in understanding the natural history of disease, suitable biomarkers, and appropriate clinical outcome measures.

Discussion

Mr. Bartek and Dr. Marks expressed appreciation to NCATS for responding to their questions about the renewal concept and conveyed their support. Mr. Bartek suggested leveraging the experience of NINDS in managing a large CTR grant program. He asked whether biomarker development and validation were differentiated in the grants and inquired about the applicant demographics. Dr. Chen explained that the NINDS CTR program is a U01 funding mechanism that addresses priority areas related to that Institute, with a 5-year award period. She added that NCATS CTR focuses on biomarkers that are close to being validated, rather than those in the early discovery phase. Academic investigators primarily comprise the CTR grant applicants, many of whom are researchers in the RDCRN.

Dr. Marks asked about plans for the CTR program beyond the concept renewal regarding sustainability. Dr. Chen noted that this program is modeling similar NCATS 3-year programs in terms of renewal cycles, with improvements embedded into the scope. Input on a direction is welcomed. Dr. Lo inquired about engaging patients and patient advocacy groups. Dr. Pariser pointed out that the CTR program is seeking to engage patients in collecting clinically meaningful outcome measures data needed for FDA approvals.

Members unanimously approved the CTR renewal concept.

XIV. ADJOURNMENT OF THE OPEN MEETING

Dr. Austin thanked the participants for their input. The next meeting is being planned for May/June 2021; the final logistics are in progress. Dr. Austin adjourned the open portion of the meeting on January 15, 2021, at 4:00 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. Date
Chair, NCATS Advisory Council
and
Director, National Center for Advancing Translational Sciences, NIH

_____ _____

Anna L. Ramsey-Ewing, Ph.D. Date
Executive Secretary, NCATS Advisory Council
Director, Office of Grants Management and Scientific Review, NCATS