

**Department of Health and Human Services
National Institutes of Health**

**National Center for Advancing Translational Sciences Advisory Council
and
Cures Acceleration Network Review Board**

**Minutes of Joint Meeting
January 16, 2020**

The National Center for Advancing Translational Sciences (NCATS) Advisory Council and the Cures Acceleration Network (CAN) Review Board held a joint meeting in open session on January 16, 2020, convening at 12:18 p.m. ET via WebEx and in Conference Room 987/989, Democracy 1 Building, at the National Institutes of Health (NIH). Christopher P. Austin, M.D., NCATS Advisory Council chair, and Ronald J. Bartek, M.A., CAN Review Board vice chair, led the meeting. In accordance with Public Law 92-463, the session was open to the public.

Prior to the joint meeting, the NCATS Advisory Council met in closed session from 11:01 a.m. to 11:34 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.

Daniel L. Hartman, M.D.

Theodore Holman, Ph.D.

Richard E. Kuntz, M.D., M.Sc.

Geoffrey Shiu Fei Ling, M.D., Ph.D.

Andrew W. Lo, Ph.D.

Brad Margus, M.B.A.

Kalpana M. Merchant, Ph.D.

Megan O'Boyle

Alan D. Palkowitz, Ph.D.

Representative Members

None present

Ex Officio Members

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

CAN REVIEW BOARD MEMBERS PRESENT

Vice Chair

Ronald J. Bartek, M.A., Co-Founder and Founding President, Friedreich's Ataxia Research Alliance (FARA)

Executive Secretary

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

Board Members

Daniel L. Hartman, M.D.	Brad Margus, M.B.A.
Theodore Holman, Ph.D.	Kalpana M. Merchant, Ph.D.
Richard E. Kuntz, M.D., M.Sc.	Megan O’Boyle
Geoffrey Shiu Fei Ling, M.D., Ph.D.	Alan D. Palkowitz, Ph.D.
Andrew W. Lo, Ph.D.	

Representative Members

Elizabeth Stoner, M.D., MPM Capital

Ex Officio Members

Khaled Bouri, Ph.D., M.P.H. (for Stephen M. Hahn, M.D.), FDA
Richard Dickinson, Ph.D., National Science Foundation

Others Present

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 at 11:34 a.m. ET.

III. CALL TO ORDER, OPEN SESSION

Dr. Austin and Ronald J. Bartek, M.A., called the meeting to order. Dr. Austin welcomed members and guests to the 23rd meeting of the NCATS Advisory Council and the 30th meeting of the CAN Review Board. He reminded attendees that the open session was being webcast. Mr. Bartek extended a welcome on behalf of the CAN Review Board, and Dr. Austin introduced the members of the Council and the Board and previewed the meeting agenda. Dr. Austin noted that the special topic presentation titled “Utilizing Artificial Intelligence/Machine Learning to Enhance Pre-Clinical Innovations” will be postponed until the May 14, 2020, Council and Board meeting.

IV. 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., confirmed the schedule for the meetings of the NCATS Advisory Council and CAN Review Board for 2020 and 2021:

- May 14, 2020
- September 17, 2020
- December 11, 2020 (virtual meeting; CAN Review Board only)
- January 14, 2021
- May 20, 2021
- September 23, 2021
- December 10, 2021 (virtual meeting; CAN Review Board only)

V. 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 2019 joint meeting.

VI. APPROVAL OF 2020 NCATS ADVISORY COUNCIL OPERATING PROCEDURES: Anna L. Ramsey-Ewing, Ph.D., Executive Secretary, NCATS Advisory Council and CAN Review Board

Dr. Ramsey-Ewing explained that the Council will need to approve the recent changes made by the U.S. Department of Health and Human Services, Office of General Council, which are reflected in the Advisory Council Charter.

Members unanimously approved the 2020 NCATS Advisory Council Operating Procedures.

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

Dr. Austin began by expressing his appreciation to seven outgoing Advisory Council and CAN Review Board members: Daniel L. Hartman, M.D.; Richard E. Kuntz, M.D., M.Sc.; Geoffrey Shiu Fei Ling, M.D., Ph.D.; Kalpana M. Merchant, Ph.D.; Valarie Montgomery-Rice, M.D.; Megan O'Boyle; and Alan Palkowitz, Ph.D. He introduced two new Advisory Council and CAN Review Board members: Theodore Holman, Ph.D., and Andrew W. Lo, Ph.D. Dr. Austin explained that because the Advisory Council, consisting of 18 members, and CAN Review Board, consisting of 24 members, serve concurrently, the terms are shorter than most groups convened under the Federal Advisory Committee Act. He announced that additional new Council and Board members will be joining pending the appointment process and approvals. Dr. Austin reported a retrospective of NCATS' fiscal year (FY) 2019 that included updates on the NCATS budget and spending and highlights on progress in some of the NCATS offices, divisions and programs. He added that this annual year in review will be longer than prior updates.

NCATS Budget: Fiscal Year 2019

Dr. Austin remarked on the strong bipartisan support of Congress for the NIH that is reflected in the increasing trend in the NIH and NCATS budgets.

- Relative to the other NIH Institutes and Centers (ICs), the NCATS final FY 2019 budget is in the middle at \$806 million in regular appropriations, which represents a steady increase since the inception of NCATS in FY 2012.

- Of the \$806 million NCATS budget, 66 percent supported the Division of Clinical Innovation (DCI), specifically, the Clinical Translational Science Award (CTSA) Program; 8 percent supported administrative costs and overhead; and the balance supported ongoing and new programs (e.g., the New Therapeutic Uses).
- Aside from the regular appropriations, \$43.9 million were transferred from the National Institute of Neurological Disorders and Stroke to NCATS in support of the Helping to End Addiction Long-termSM Initiative, or NIH HEAL InitiativeSM.

Office of Grants Management and Scientific Review: Fiscal Year 2019 Metrics

Dr. Austin pointed out that approximately 85 to 90 percent of the NCATS budget (roughly \$700 million) is allocated in grants, contracts and other extramural funding mechanisms. The Office of Grants Management and Scientific Review (OGMSR), under the leadership of Dr. Ramsey-Ewing, manages and oversees these activities. Dr. Austin described the OGMSR FY 2019 activities.

- **The Office of Scientific Review (OSR)** staff of six conducted peer reviews of 283 grant applications requesting \$1.5 billion and 22 contract proposals requesting \$117 million. Prior to initiating the formal review process, the OSR contacted more than 2,000 potential reviewers and recruited 578 reviewers to 28 review panels covering 45 days of meetings.
- **The Office of Grants Management (OGM)** begins its work and coordinates with other financial offices within the NIH after a concept is approved. The OGM staff negotiated and issued 547 awards obligating \$956 million and reviewed 48 Funding Opportunity Announcements (FOAs) servicing NCATS, as well as the Office of Research Infrastructure Programs, *All of Us* and the Common Fund.

Clinical and Translational Science Award Program

Dr. Austin noted that the funding obligations by fiscal year and award type or funding mechanism for the Clinical and Translational Science Award (CTSA) Program, with embedded links to the NIH Research Portfolio Online Reporting Tools (commonly called RePORT), can be accessed from the NCATS website: <https://ncats.nih.gov/files/ctsa-funding-information.pdf>. NCATS investments in the CTSA program significantly increased in the past 5 years, from \$477.2 million in FY 2014 to \$559.7 million in FY 2019.

- **CTSA Program Hub Awards.** NCATS issued 11 new Hub awards, two of which—Rutgers Biomedical and Health Sciences and the University of Virginia—were first-time CTSA Hubs.
- **CTSA Program Administrative Supplements: Enhancing Network Capacity (PA-16-328).** NCATS awarded six new administrative supplements to existing grants to continue efforts of fostering dissemination of local Hub innovations among the 60 funded CTSA. The topics focused on rural health, community engagement, and training and education.
- **CTSA Collaborative Innovation Awards (CCIA).** NCATS issued nine new CCIA awards consisting of six U01 awards and three new R21 awards to catalyze collaborations among 25 distinct academic and research institutions. Projects focus on the opioid epidemic, congenital anomalies, drug repurposing, telehealth, informatics and workforce training.

- **CTSA Program Diversity and Re-entry Research Supplements.** Dr. Austin conveyed NCATS' commitment to translational research workforce diversity and acknowledged the eight new FY 2019 awardees.

For FY 2020, Dr. Austin explained that NCATS will be initiating Competitive Supplements in the CTSA Program; issuing a new Hub FOA with input from the research community (internal and external); and proposing a CTSA Operations Contract, which will be discussed as a concept later in the meeting.

Office of Rare Diseases Research Update

Dr. Austin provided a brief update on the activities of the Office of Rare Diseases Research (ORDR).

- **Rare Diseases Clinical Research Network (RDCRN).** Dr. Austin reminded the Council and Board that the RDCRN is a network of multisite, multidisciplinary consortia that each focus on three or more rare diseases that have a biological or medical characteristic in common. The Network began its fourth 5-year cycle of funding (i.e., RDCRN4) in FY19. A Data Management and Coordinating Center was awarded to the Cincinnati Children's Hospital Medical Center, and five new areas of emphasis were added to the RDCRN4.
- **The Clinical Trial Readiness (CTR) Program.** NCATS in collaboration with the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) issued the first CTR grants for rare diseases, disorders and syndromes and funded seven clinical projects: six Exploratory/ Developmental Research Grant (R 21) awards through NCATS and one Small Research Grant (R03) award through NICHD.
- **Rare Disease Day (RDD) at NIH.** In support of International RDD, NCATS sponsors the annual RDD at NIH, and this year's event will be held on February 28, 2020. Dr. Austin remarked on the enthusiasm and the record-breaking attendance of prior RDD events.

Division of Pre-Clinical Innovation

Dr. Austin informed the Council and Board that the NCATS Chemical Genomics Center (CGC; originally the NIH CGC) was renamed the Early Translation Branch. The Division of Pre-Clinical Innovation (DPI) continues its record of productivity with 178 collaborative projects—each representing a different disease, target or organ system—being reported in the NIH Intramural Database in FY 2019. The number of publications being produced also remains above average, and these publications are appearing in high-impact journals. Dr. Austin highlighted some of the FY 2019 DPI collaborative projects and accomplishments.

- **Developing Drug Combination Therapy for Diffuse Intrinsic Pontine Glioma (DIPG).** An invasive inoperable brain stem tumor primarily treated with radiation, DIPG is diagnosed in 450 pediatric patients with median age of 6.3 years annually; 90 percent of the children die within 2 years of a diagnosis, and only 1 percent survive past 5 years. In this project, six unique patient-derived DIPG cell lines developed in teamwork among multiple NCATS groups and external collaborators at Stanford University and Johns Hopkins University were screened against potential drug candidate compounds. Two active compounds (i.e., top hits), a known FDA-approved cancer therapeutic in clinical trials since 2016 (panobinostat) and the only known blood-brain barrier penetrant proteasome inhibitor (marizomib), were identified and further screened for combination drug synergy, revealing five hotspots. Both panobinostat and

marizomib alone and in combination were effective in animal studies. The DIPG project has resulted in two ongoing clinical trials evaluating panobinostat, and data are being published. All screening data are publicly available in NIH's PubChem. The next steps will be to complete the FDA investigational new drug (IND) submission for marizomib. In anticipation of FDA approvals, clinical trials for testing panobinostat/marizomib combinations are planned at three sites: Dana-Farber Cancer Institute, Stanford University and Oregon Health & Science University. Dr. Austin elaborated on the publicity that this project has received and the collaborative effort, skill and ingenuity that has taken the near-hopeless DIPG to a potentially treatable cancer. He noted that this approach has broad application to many other diseases beyond cancer.

- **Therapeutic Development Branch (TDB).** Dr. Austin was happy to report that nine project INDs were filed in FY 2019 from the TDB programs: three in the Therapeutics for Rare and Neglected Diseases (TRND) program and six in the Bridging Development Gaps (BrIDGs) program. Each of the INDs is focusing on poorly treatable diseases, and some are enabling critical studies in humans. This work is addressing the issue of treating more patients rapidly and was completed with a budget of \$30 million, which is significantly less than the industry trends.
- **Protein Replacement Therapy for Friedreich's Ataxia (FA).** Dr. Austin explained that FA is a recessive inherited disorder caused by a deficiency in the mitochondrial protein, frataxin (FXN), and affects one in 50,000 people. No approved treatments for FA exist, current therapies are symptomatic management focused, and conventional protein replacement approaches are ineffective. This Indiana University School of Medicine-led project, in collaboration with the NCATS TRND team, investigated (FY 2015 to FY 2018) an alternative strategy of using a cell-penetrant fusion peptide (CTI-1601) to deliver functional FXN to the mitochondrial matrix. The mature project advanced from TRND after Series A funding by Chondrial Therapeutics. The company then completed the pre-clinical studies, filed the IND with the FDA, and is performing, in FA patients, the first in-human trial of CT-1601. Dr. Austin noted that FARA has long supported this program.

NCATS' Role in the NIH HEAL Initiative

Dr. Austin explained that NCATS is using its innovative breakthroughs, platforms and technologies to address a difficult problem of pain management in response to the opioid crisis. NCATS' involvement in the NIH HEAL Initiative consists of three main areas: pre-clinical research in pain, clinical research in pain management and expanding therapeutic options.

- **Drug Development and Testing Platform.** Six different agendas comprise the pre-clinical research in pain component to support the NIH HEAL Initiative and leverage existing DPI programs, including the 3-D Tissue Bioprinting, Tissue Chips for Drug Screening, and A Specialized Platform for Innovative Research Exploration (ASPIRE) Programs. Both indications, addiction (55%) and pain (30%), are represented in the current NCATS-NIH HEAL Initiative portfolio. The portfolio includes applicants from all sectors (e.g., academia, government, industry), and technologies are generally at the same stage in the drug development pipeline.
- **NIH HEAL Initiative: Pain Management Effectiveness Research Network (Pain-ERN or ERN).** Six Pain-ERN clinical trials are being launched to test pain conditions and interventions—including musculoskeletal, acute and chronic pain.

Looking Ahead to the Remainder of FY 2020 and FY 2021

Dr. Austin remarked that the FY 2020 budget was signed into law on December 20, 2019 and includes a 6 percent increase for the NIH (\$2.3 billion) and a 3 percent increase for NCATS (\$27 million) above the FY 2019 enacted budget. The President's FY 2021 Budget proposal is expected to be released on February 10, 2020, and Congressional hearings likely will be scheduled sometime between March 2020 and May 2020. Congressional bills then will follow in the summer of 2020.

Discussion

Mr. Bartek inquired about the difference in the CAN FY 2019 enacted budget of \$44.5 million, which is less than the proposed amount of up to \$80 million. Dr. Austin clarified that the \$44.5 million represented the amount of funds actually dispersed, not the budgeted amount. Although authorized, the NCATS FY 2019 budget increase did not allow spending a full \$80 million.

Mr. Bartek lauded the NCATS for a successful FY 2019, especially in having the infrastructure and resources to enable submitting nine INDs to the FDA. Dr. Austin commented on the NCATS' programs' scale of translation that is realized as fold, rather than percentage, increases; the TDB had a fivefold increase in productivity in FY 2019, which affects the public and private sectors, translating to medicines' being made available to patients sooner.

Ms. O'Boyle asked about examples of across-disease research that has resulted in actionable recommendations. Dr. Austin commented that many of the DPI projects have the potential to address multiple indications. He highlighted an ongoing collaboration with the National Institute of Mental Health, National Institute on Aging and University of Maryland on a BrIDGs project evaluating an orally bioavailable ketamine metabolite that is effective in treating drug-resistant depression with minimal hallucinogenic side effects. The goal is to test this drug, which could potentially be efficacious in multiple clinical indications, such as anxiety, pain and posttraumatic stress disorder.

VIII. INTRODUCTION OF NEW STAFF: Keith R. Lamirande, M.B.A., Associate Director, Office of Administrative Management, Executive Officer, NCATS; Emily Carlson Marti, M.A., Director, Communications Branch, Office of Policy, Communications and Education (OPCE), NCATS

Keith R. Lamirande, M.B.A., announced the appointment of Andrew Kelly, M.B.A., as budget officer and chief, Financial Management Branch, who has served as NCATS deputy budget officer since October 2016. Mr. Lamirande also announced that NCATS' current budget officer, George J. Coy, will be retiring in February 2020 and expressed his appreciation to Mr. Coy for his service.

Emily Carlson Marti, M.A., introduced Sarah B. Berson, J.D., as a new writer/editor, OPCE Communications Branch. Ms. Berson comes to NCATS from the private sector as a contractor and has supported the NIH and other federal agencies as a project director and writer/editor.

IX. CLEARANCE OF CONCEPTS

The Council and Board received presentations on four new projects 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.

Clinical and Translational Science Award Program Operations Support: Clare K. Schmitt, Ph.D., Deputy Director, DCI, NCATS

Clare K. Schmitt, Ph.D., presented a contract concept for operations support for the CTSA Program—related grantee and NCATS staff activities. Dr. Schmitt reminded the Council and Board that the CTSA Program is a national network of medical research institutions and their partners and collaborators and, as of FY 2019, has 60 active primary sites. The aims of the Program are to accelerate translation of research discoveries into improved care for patients by addressing systemwide clinical and translational research problems collaboratively; disseminate the expertise, tools, training and clinical research innovations for effective treatments; and support a diverse translational science workforce.

The goal of this operations support contract concept is to provide effective and efficient management of this large, complex national CTSA Program, including the ongoing administrative tasks (e.g., supporting the consortium-wide agendas and large-scale Program deliverables). Specific operations support tasks will include transfer of the NCATS Specific, Measurable, Achievable, Realistic, and Timetable (SMART) institutional review board (IRB) platform from the current grantee for long-term management and receipt and distribution of funds from other ICs and sister agencies for emergent clinical trial needs. In addition, the operations support contract will provide meeting and conference support and manage data safety monitoring—related activities in clinical trials.

The expected outcomes will be the consolidation of multiple activities under one contract and addition of needed tasks, allowing grantees to focus their intellect and efforts on addressing the CTSA Program goals and, therefore, NCATS goals. Regarding plans to promote and ensure sustainability, the activities and platforms will be hosted on the NCATS cloud platform, so a transition plan is required.

Discussion

Dr. Palkowitz remarked on the success, growth and complexity of the CTSA Program and the need to harmonize practices across the consortium, which this concept is anticipated to achieve. Aside from establishing a central management structure, the operations contract will remove the administrative workload away from CTSA researchers and NCATS staff, allowing added focus on the science, all of which he thinks are important steps in the Program moving forward.

Dr. Hartman expressed his support for the concept and appreciates NCATS' focusing efforts on new initiatives that, once established, will be managed outside of the Center. Dr. Hartman asked how the data safety monitoring expertise would be addressed in the contract. Dr. Schmitt explained that the concept is still in the early planning phase and pointed out that multiple contracts may be required to fulfill all of the goals and specific tasks. Data safety monitoring is one area that NCATS is reviewing and may need assistance with.

In response to a question about the magnitude of resources the CTSA Program receives from ICs, Dr. Schmitt replied that managing other IC resources is one task NCATS is hoping to carry out effectively as it aims to build and fund the necessary infrastructure.

Ms. O'Boyle expressed enthusiasm for the SMART IRB but was unclear on whether an academic contractor would serve as manager. Dr. Schmitt clarified that the FOA will explain the needs, and any applicant (academia or industry) able to provide those services will be considered, as well as the prime and subcontractor arrangements.

Members unanimously approved the CTSA Program operations support concept.

Biomedical Translator—User Interface (UI) Development: Christine M. Colvis, Ph.D., Director, Drug Development Partnership Programs, NCATS

Christine M. Colvis, Ph.D., presented a contract concept for developing a UI for the NCATS Biomedical Translator (Translator). Approved in December 2015, the Translator program aims to enable exploring computationally assisted knowledge graphs and constructing new research hypotheses. NCATS has completed the feasibility phase of Translator and moved to the development phase. Dr. Colvis explained that NCATS has invested in user-centered design work for the UI, but not its development.

The goals of this concept are to develop an agile UI for Translator that will allow the broader research community to use Translator and provide researchers the ability to query the data system for key information for addressing research questions. NCATS recognizes that proper execution of user-interface design will require collaboration involving a team with expertise in user-centered design and biomedical science. In 2019, NCATS engaged the 18F (an abbreviation for 1800 F Street) Office, Technical Transformation Services, General Services Administration, to conduct user-centered design research and identify core use cases. The 18F report recommended engaging interface developers through a contract mechanism.

Aside from delivery of a Translator UI that is intuitive for researchers, other expected outcomes will be an unprecedented view of biomedical information and data presentations that enhance human reasoning and understanding of specific aspects of medicine, both biologic and physiologic. No broadly used system like Translator currently exists elsewhere. All results and software developed will be publicly available through GitHub. For the long term, Translator aims to foster community-driven adoption of data-sharing standards and practices.

Discussion

Dr. Kuntz is supportive of the concept on developing the Translator UI, but he commented that it seems overly ambitious. He wondered whether “translation” in this context is referring to the utility of data aggregation and combined analyses, given that much has been done in the area of data curation. Dr. Colvis clarified that Translator uses existing and primarily curated data. She elaborated that through data linkages, connections and associations to what occurs in the human body, Translator is well equipped to address adverse effects and drug repurposing and to provide new insights into drug mechanisms and links to signal transduction pathways.

Dr. Ling expressed his enthusiasm and strong support for the concept, emphasizing the aspirational nature of the Translator project befitting NCATS’ model. The idea of bringing disparate data together in a way that is meaningful to inform clinician decision-making addresses a critical need. Given that the success metrics are milestone-driven, Dr. Ling noted the importance of also having a time constraint built into the contract mechanism. Dr. Colvis pointed out that Translator, at this initial stage, primarily is targeted to translational researchers, but also is used by practicing clinicians to find solutions to extremely rare, undiagnosed disease cases.

Members unanimously approved the biomedical translator UI development concept.

Supporting Clinical Trials of a Prime Genome Editor in Multiple Genetic Diseases: P.J. Brooks, Ph.D., Program Director, ORDR, NCATS

P.J. Brooks, Ph.D., presented the concept of supporting clinical trials of a prime editor (e.g., CRISPR) for the treatment of multiple genetic diseases. The current approach to gene-editing clinical trials is focusing on one disease at a time. This approach is based on commercial considerations, which is not optimal for addressing the thousands of rare monogenic diseases that exist. In 2019, researchers discovered a modified CRISPR Cas9 (CRISPR-associated protein 9) technology that has the potential to correct 90 percent of human disease-causing mutations without introducing double-strand DNA breaks or increasing the risk of cancer. The DCI and ORDR are interested in expanding these findings to NCATS programs and clinical trials.

The concept goals are to assess the feasibility of clinical trials of a prime editor in multiple rare monogenic diseases and identify and overcome any feasibility challenges for such trials. Dr. Brooks emphasized that the concept would leverage ongoing efforts, such as the NCATS CTSA Program and the NIH Common Fund Somatic Cell Genome Editing program. This initiative will use the general framework of the CCIA program and will support clinical trials that focus on defects in a somatic cell type to which a single prime editor can be delivered (e.g., liver hepatocytes). Depending on the technology delivery method, potential regulatory issues involving the FDA Center for Biologics Evaluation and Research may need to be addressed.

Several outcomes are expected, including identifying and overcoming challenges in conducting these types of clinical trials, increasing the number of rare disease patients in trials, and maximizing the clinical impact of somatic genome editing. If successful, this project will fundamentally change the way genome editing in rare diseases clinical trials are conducted. Results will be disseminated to both the gene editing and rare disease research communities via the CTSA Program and publications. Ultimately, the goal is to identify a regulatory pathway for clinical trials of a prime editor that includes rare disease patients.

Discussion

Ms. O'Boyle expressed her support for the concept, which is filling a gap in cross-disease research. She asked whether the CTSA's routinely work with patient advocacy groups and noted the work that needs to be completed before a first clinical trial. Dr. Michael G. Kurilla, director, DCI, NCATS, which houses the CTSA Program, pointed out that many CTSA's are led by pediatricians who have active rare disease programs and engage patient advocacy groups and other foundations specific to the disease that they treat and study. Dr. Brooks added that RDCRN investigators are at CSTA Hubs and explained that the modified CRISPR editor recently was discovered and efficacy demonstrated in a laboratory, rather than a clinical setting. A significant amount of work will be necessary before the first human study can be initiated.

Dr. Ling remarked that this is another potential NCATS success that would have tremendous impact and also expressed his support for the concept, acknowledging that advancing a product from bench to bedside takes time.

Members unanimously approved the clinical trials for multiple genetic diseases and prime genome editor concept.

**SaME Therapeutics—Clinical Trials of Drugs Targeting Shared Molecular Etiologies in Rare Diseases:
P.J. Brooks, Ph.D., Program Director, ORDR, NCATS**

Dr. Brooks presented the concept of supporting rare diseases clinical trials of drugs targeting SaME therapeutics. Although thousands of rare diseases exist, the number of underlying causes (i.e., etiologies) is small. The SaME approach is the focus of ongoing drug development. In addition, drugs targeting SaME in different cancers are considered state-of-the-art in oncology, and the approach has established a regulatory pathway for these types of FDA drug approvals. Although discussion and interest in SaME for rare diseases have increased in the Collaborative Forum on Rare Diseases and the International Rare Disease Research Consortium, no clinical trials are ongoing.

The goals of the concept are to adapt the oncology SaME approach to rare diseases and identify and overcome any challenges. It is anticipated that recruiting for clinical trials based on SaME will dramatically increase the number of rare disease patients in trials, translating to more treatments delivered to more patients more rapidly. The concept will leverage the RDCRN, and the results will be disseminated to the community via this Network and publications. The expected outcome will be the ability to stratify patients according to underlying etiology rather than traditional clinical characteristics, thus transforming rare disease clinical trials.

Discussion

Ms. O’Boyle and Dr. Kuntz are in support of this concept, which addresses multiple rare diseases simultaneously. In response to a question on whether different protocols will be used depending on the disease, Dr. Brooks explained that the project aims to identify the necessary protocols that will be effective. The objective is to focus on the underlying molecular etiology that can be corrected with targeted SaME.

Members unanimously approved the SaME therapeutics and rare diseases clinical trials concept.

X. CURES ACCELERATION NETWORK REVIEW BOARD UPDATE: Ronald J. Bartek, M.A., Co-Founder and Founding President, FARA, Vice Chair, CAN Review Board

Mr. Bartek presented an overview of the December 2019 CAN Review Board meeting, including brief updates on the two CAN Project Proposals: (1) Gene Therapy Program and (2) Repurposing Generic Drugs. He detailed establishment of the CAN Review Board Working Group, the charge and the upcoming activities.

CAN Project Proposal 1: Gene Therapy

Mr. Bartek conveyed that during the past year, the gene therapy program has participated in four workshops; two are planned for 2020.

- NCATS and FDA will co-host the “Workshop on Expanding Adeno-Associated Virus (AAV) Manufacturing Capacity for Rare Disease Gene Therapies” on January 28–29.
- NCATS will host the “Workshop on Systemic Immunogenicity Considerations” on July 7–8.

Mr. Bartek emphasized the need to implement efficient, cost-effective manufacturing methods for gene therapy. He urged the attendees to consider methods to address the issues of gene therapy through fundable projects.

CAN Project Proposal 2: Repurposing Generic Drugs

Mr. Bartek spoke also on the drug repurposing program. He highlighted the “Repurposing Off-Patent Drugs: Research and Regulatory Challenges” workshop, which was held December 5–6, 2019, and was co-sponsored by the FDA, NCATS and the Reagan-Udall Foundation. He conveyed that the workshop enabled the development of a task force to address forward-leaning ideas about solutions in drug repurposing.

CAN Program Updates and Clearance of CAN Concept

Mr. Bartek highlighted that several CAN programs were discussed at the December 2019 CAN Review Board meeting, including the Platform Vector Gene Therapy Project, Biomedical Data Translator, ASPIRE and Tissue Chips for Drug Screening Program. Additionally, a CAN concept clearance was approved to advance a conference grant for the implementation of tissue chips.

CAN Review Board *Ad Hoc* Working Group Planning Meeting

The CAN Review Board and NCATS discussed and agreed on establishing a CAN Review Board *ad hoc* Working Group devoted to identifying methods to advance mature NCATS projects to real-world applications (i.e., clinical practice). Mr. Bartek elaborated on how CAN then would become the thoroughfare for implementing translational science, and he described the activities in two key areas: planning and addressing bottlenecks. For planning, Mr. Bartek emphasized raising awareness and strengthening partnerships with stakeholders, setting decision parameters, setting priorities, and facilitating project adoption. Obvious bottlenecks to be addressed include budget variability and caps, stakeholder involvement, and mechanisms for deciding which projects to advance.

Regarding the charge, NCATS seeks recommendations that will enable the Center to better leverage the power of CAN and its authorities to speed transformational science and foster its implementation and staying power. To address this charge, the Working Group will review and assess the CAN authorities, provide input on project prioritization and phase-out, identify long-term sustainability strategies, and identify factors to enhance stakeholder engagement. The Working Group will meet virtually and in-person; specific dates are to be determined. The first CAN Review Board leadership and Working Group Co-Chairs biweekly teleconference is scheduled for January 17, 2020, and members will discuss filling the roster.

At the first Working Group meeting, NCATS program officers will present some of the CAN projects, addressing their history, current status and challenges. Topics of discussion will include CAN support, defining success, challenges to success, long-term sustainability, stakeholder roles and lessons learned for future projects. Working Group members also will be tasked with identifying scientific areas of improvement. Topics of discussion will include speed, organizational practices and suggestions for improvement.

Mr. Bartek called attention to key themes of the December 2019 planning meeting discussion: (1) dissemination of deliverables; (2) recommendations to address issues related to policies, programs and procedures; (3) bringing multiple perspectives to the table; (4) consideration of synergy among CAN projects; (5) identification of barriers; (6) better planning for budget variability; (7) considering specific authorities and how they have been used by other agencies; and (8) considering and optimizing stakeholder engagement.

Discussion

In response to an inquiry from Dr. Austin, Mr. Bartek affirmed that the Working Group roster will be finalized at the January 17, 2020, meeting. Dr. Austin expressed his enthusiasm regarding the Working Group and expressed appreciation for the members' diverse perspectives.

Dr. Lo commented on the great opportunity and asked about the CAN Review Board mandate regarding dissemination of business models to parents and patient advocates. Dr. Lo added that platform trials—focused on multiple diseases with a single molecular etiology—were optimal from a business perspective. Mr. Bartek clarified that the Working Group membership will include business partners and invited Dr. Lo to share his expertise with the CAN Review Board and NCATS leadership.

Dr. Austin posed a pivotal question on whether the CAN Review Board should consider financing business models. Dr. Lo commented that researchers often are unaware of opportunities for business modeling. He stated that NCATS is positioned to provide guidance on implementing clinical technologies into commercially viable entities. Ms. O'Boyle commented on the urgency of finding solutions for diseases. She conveyed that base funding is essential, particularly for family-based organizations. Elizabeth Stoner, M.D., expressed her support for developing a financial model, noting that education and partnerships will be crucial.

Action Item: The CAN Review Board and NCATS leadership will discuss developing a financial business model for advancing CAN projects.

XI. NCATS SMALL BUSINESS INNOVATION RESEARCH AND SMALL BUSINESS TECHNOLOGY TRANSFER PROGRAM UPDATE: Lili M. Portilla, M.P.A., Director, Office of Strategic Alliances, NCATS

Lili M. Portilla, M.P.A., provided an update of the NCATS Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) programs. SBIR and STTR represent one of the largest sources of early-stage financing across federal agencies; the NIH allocated \$1.15 billion in 2019 for the programs. Ms. Portilla explained that SBIR is designed to promote federal research and development engagement; STTR facilitates cooperative research and development between small business concerns and U.S. research institutions.

The benefits of the SBIR and STTR programs include stability, predictability, retention of intellectual property rights and technical assistance. Ms. Portilla explained that the projects undergo a rigorous scientific peer review process, and awards can be leveraged for other funding and collaborative opportunities. SBIR and STTR operate in three phases: (1) a feasibility study, (2) full research and competing renewal, and (3) commercialization.

NCATS receives most of its applications through an Omnibus Solicitation (i.e., investigator-initiated grant funding). Other avenues include grant solicitations in targeted areas (i.e., grants to advance a particular technology or research area) or SBIR contract solicitations (i.e., contract opportunities to advance areas of high research interest). Most NCATS SBIR and STTR funding is allocated to tools for drug discovery and development (44%) and bioinformatics (25%). Other areas include rare diseases (16%), clinical research tools (12%) and devices (3%).

Program applications have increased since FY 2013, resulting in part from the establishment of an outreach contract in March 2014. Ms. Portilla spoke on efforts to engage stakeholders with an interest

in the programs. She emphasized the importance of contacting and supporting applicants, noting that many applicants lack grant writing experience and institutional support. Ms. Portilla also highlighted specialized efforts to support women- and minority-owned small businesses.

Ms. Portilla highlighted four NCATS SBIR success stories:

- **IonField Systems** developed and commercialized an automated microplate cleaner. The initiative saved hundreds of thousands of research dollars and reduced environmental plastic waste. The company recently announced the first installation of a commercial release.
- **Recursion Pharmaceuticals** received support to model 2,000 genetic diseases in multiple human cell types. The company since has attracted more than \$100 million in investments and strategic partnerships with Sanofi Genzyme and the Takeda Pharmaceutical Company.
- **AxoSim, Inc.** facilitates the prediction of neurological safety and efficacy early in the drug development pipeline. The company is establishing partnerships with pharmaceutical companies for application of the platform.
- **Lyndra Therapeutics** is developing oral, ultra-long-acting, sustained-release therapies. An NCATS SBIR grant helped the company improve its manufacturing ability.

The strategic approach for outreach objectives includes (1) articulating key messages and research topics of interest; (2) partnering with state associations, academic centers and specialty organizations; (3) expanding social media presence and engagement; (4) engaging with potential applicants and third-party influencers; and (5) expanding outreach. Ms. Portilla invited the attendees to provide input on prioritization, outreach and improvement.

Discussion

Dr. Holman spoke on NCATS SBIR/STTR program's support for grant writing, responding to criticisms and resubmissions. Ms. Portilla agreed, noting the importance of encouraging resubmissions, particularly from female entrepreneurs, who often exhibit low re-submission rates.

Dr. Lo suggested that NCATS pursue strategies to communicate success stories to the public, noting that videos often are effective. Dr. Hartman echoed Dr. Lo's statement, adding that information on the programs must be easily accessible.

Action Item: Ms. Portilla and the Office of Strategic Alliances will consider developing videos to feature success stories from the SBIR program.

Mr. Bartek commented on the importance of coordination of the SBIR and STTR programs within NCATS. He noted that the program objectives are aligned closely with NCATS' mission. Ms. Portilla added that the programs are designed to leverage NCATS research efforts.

Dr. Austin asked whether development of financial models within the SBIR and STTR programs is possible. The attendees discussed methods to encourage partnerships and collaborations with nonprofit organizations. Ms. O'Boyle suggested that opportunities for outreach and communication be presented at RDD at NIH.

Action Item: The Office of Strategic Alliances will (1) consider including presentations on partnerships and collaborations with nonprofit organizations at future NCATS events (e.g., RDD at NIH) and (2) explore new opportunities for partnerships in the SBIR and STTR programs.

Anne Pariser, M.D., highlighted the need to relieve the financial burden of families with children who have rare diseases. Mr. Bartek and Ms. O’Boyle reiterated the value of partnerships in addressing this issue. Penny Burgoon, Ph.D., suggested further discussions on the financial aspects of translational science.

Action Item: The Office of Strategic Alliances will consider presenting rare disease case examples from patient groups to small businesses.

XII. ADJOURNMENT OF THE OPEN MEETING

Dr. Austin thanked all of the participants for their input. Dr. Austin and Mr. Bartek adjourned the open portion of the meeting at 3:52 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

Ronald J. Bartek, M. A.
Vice Chair, Cures Acceleration Network Review Board;
and
Founding President, Friedreich’s Ataxia Research Alliance

Date