Department of Health and Human Services
National Institutes of Health
National Center for Advancing Translational Sciences
37th Meeting of the
Advisory Council

Minutes of Hybrid Meeting
September 19, 2024

The National Center for Advancing Translational Sciences (NCATS) Advisory Council held a meeting in open session on September 19, 2024, from 11:16 a.m. to 5:05 p.m. ET, via National Institutes of Health (NIH) VideoCast and in Seminar Room 110, 9609 Medical Center Drive, Rockville, MD. Joni L. Rutter, Ph.D., NCATS Advisory Council Chair, led the meeting. In accordance with Public Law 92-463, the session was open to the public.

Prior to the meeting, the NCATS Advisory Council met in closed session on September 19, 2024, from 9:01 a.m. to 10:11 a.m. ET, for the review and consideration of grant applications.

NCATS ADVISORY COUNCIL MEMBERS PRESENT

Chair

Joni L. Rutter, Ph.D., Director, NCATS

Executive Secretary

Anna L. Ramsey-Ewing, Ph.D., Director, Division of Extramural Activities (DEA), NCATS

Council Members

Sergio A. Aguiar-Gaxiola, M.D., Ph.D.
Paul A. Harris, Ph.D.
Annie M. Kennedy, B.S.
Kelly Marie McVearry, Ph.D., Ed.M.
Robin J. Mermelstein, Ph.D.
Keith J. Mueller, Ph.D.
Paula K. Shireman, M.D., M.B.A.

***Ad Hoc* Council Members**

None present

Representative Members

None present

***Ex Officio* Members**

None present

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 provisions of Public Law 117-286.

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.

Review of Grant Applications

The Council reviewed 62 research, research-related, and training grant applications with primary assignment to NCATS for a requested amount of $40,044,171 in first-year direct costs. The Council concurred with the recommendations of the initial review groups. For the record, it is noted that applications with secondary assignment to NCATS were also considered.

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

Joni L. Rutter, Ph.D. adjourned the closed session of the NCATS Advisory Council meeting on September 19, 2024, at 10:11 a.m. ET.

III. CALL TO ORDER, OPEN SESSION

Joni L. Rutter, Ph.D. called the meeting to order and welcomed members and guests to the 37th meeting of the NCATS Advisory Council. Anna L. Ramsey-Ewing, Ph.D., conducted the roll call and reviewed the meeting agenda. She noted the meeting logistics and reminded attendees that the open session was being livestreamed on NIH VideoCast.

IV. CONFIRMATION OF DATES FOR FUTURE NCATS ADVISORY COUNCIL MEETINGS: Anna L. Ramsey-Ewing, Ph.D., Director, Division of Extramural Activities, NCATS; Executive Secretary, NCATS Advisory Council

Anna L. Ramsey-Ewing, Ph.D. confirmed the schedule for the meetings of the NCATS Advisory Council for 2025 and 2026:

- January 30–31, 2025 (virtual meeting)
- May 22–23, 2025
- September 18–19, 2025
- January 29–30, 2026 (virtual meeting)
- May 21–22, 2026
- September 17–18, 2026

V. DIRECTOR'S REPORT: Joni L. Rutter, Ph.D., Director, NCATS; Chair, NCATS Advisory Council

Joni L. Rutter, Ph.D. began by providing a recap of the May 2024 meeting. During that meeting, she conveyed that NCATS leadership is in place and that NIH's search for a director of the National Library of Medicine would close on July 1, 2024. She indicated that the fiscal year 2024 (FY24) budget was enacted and that NCATS received a $5 million increase above the FY23 enacted budget. In addition, discussions were underway on the FY25 budget. NCATS has made several impactful advances and received a thank-you proclamation from the Cure Juvenile Myositis advocate community. NCATS activities have gained interest from Congress, and discussions with the U.S. Food and Drug Administration (FDA) and European Medicine Agency are ongoing. Increased Cures Acceleration Network (CAN) support bolstered gene therapy for methylmalonic acidemia and increased research in other CAN-related activities. The draft Strategic Plan is out for final comments. The Council heard updates from the FDA and program updates

from the NCATS Division of Rare Diseases Research Innovation (DRDRI) and Division of Preclinical Innovation (DPI).

After this review of the previous meeting, Dr. Rutter announced NCATS staff changes, provided Council updates, reported on the FY25 budget, and highlighted progress in some of the NCATS offices, divisions, and programs. She also provided a brief update on the *NCATS Strategic Plan for 2025–2030*.

NCATS Staff Changes and Recruitments and Council Updates

Dr. Rutter announced that NCATS has filled several leadership positions across divisions and offices since the last Council meeting. A search for a new NCATS executive officer in the Office of Administrative Management is underway. Dr. Rutter expressed appreciation to Bekah Geiger, M.S.W., deputy executive officer, who has been serving as acting executive officer.

Dr. Rutter welcomed NCATS' new deputy director and former Council member, Annica M. Wayman, Ph.D. Dr. Wayman noted that she has a blend of experiences in her background that tends toward translational science. She is an engineer and has conducted research in biophysics in the private sector and in government. Dr. Wayman started the Bachelor of Science in Translational Life Science Technology program at University of Maryland, Baltimore County where she worked before joining NCATS. She is excited to work alongside Dr. Rutter and NCATS' staff, all of whom are passionate about the mission of NCATS. Dr. Wayman commends NCATS' work, which she observed as a Council member, and welcomes the opportunity to observe NCATS on a deeper level. She looks forward to implementing the *NCATS Strategic Plan* in the future directions of NCATS and understanding ways to better leverage the Council in NCATS' activities.

Dr. Rutter extended a farewell and appreciation to Council member Annie M. Kennedy, B.S., who has completed her tenure.

NCATS Fiscal Year 2025 Budget

Dr. Rutter reported that President Joseph R. Biden released the FY25 budget proposal on March 11, 2024, and requested $926.1 million for NCATS, which is a 0.3 percent increase in appropriations above the FY23 enacted budget. She reminded the Council that the President's FY25 budget proposal was released before the FY24 budget approval and was, therefore, based on the FY23 appropriation levels. The House and the Senate both have drafted bills that have passed their respective appropriations committees, but the bills have not been passed out of the full committees. The fiscal year ends on September 30, 2024, and a continuing resolution (CR) will be needed to fund the government beginning October 1, 2024, if the FY25 budget is not approved. NCATS is optimistic that if a budget is not approved, a CR will be executed to prevent a lapse in funding in the government. The House has proposed a CR that would extend through March 28, 2025. Further details on NCATS' budget and related activities can be found on the center's Budget webpage.

News and Announcements

Dr. Rutter highlighted recent NIH-wide and NCATS-specific announcements and events.

- **Assay Guidance Manual (AGM) Program Workshops.** On September 24 and 25, 2024, the NCATS AGM program and Eli Lilly and Company will co-host an Assay Guidance Workshop for High-Throughput Screening and Lead Discovery. On October 23 and 24, the AGM program will host an *In Silico* Drug Discovery workshop, which emphasizes NCATS' interest in new approach methodologies . The AGM workshops have successfully convened the scientific community and provided guidance on various translational topics. All workshops are virtual and free to attend.

- **Visits to NIH and NCATS.** On September 10, 2024, The 2024 Mansfield-PhRMA Research Scholars program cohort visited NCATS. Each year, through this U.S.–Japan exchange program, early career pharmaceutical scientists from Japan visit the United States to learn about translational science. The scholars visited NCATS, toured NCATS laboratories, and heard from transitional scientists about several projects. The main goal is to share best practices and exchange information. NCATS aims to build international relationships and promote scientific diplomacy worldwide to enable more collective scientific advances. On September 18, 2024, organized by the French Embassy and the Counselor of Science and Technology, representatives from the Paris Brain Institute visited NCATS and the National Institute of Neurological Disorders and Stroke. They discussed potential collaborations overlapping with translational science and brain research, including topics related to neurological and psychiatric disorders and partnership opportunities. Dr. Rutter emphasized engaging with individuals and groups with similar research interests over time and building those relationships. Again, NCATS' main goal is to share best practices and exchange information.

- **Congressional Briefings and Activities.** NCATS has taken opportunities to visit with Congress during briefings on Capitol Hill to discuss and showcase ongoing programs and initiatives. On July 25, 2024, Dr. Rutter and other NCATS staff joined legislators at a showcase of artificial intelligence (AI) initiatives. They shared updates on the National COVID Cohort Collaborative (N3C), 3-D modeling, and AI/machine learning (ML) projects with members of the Senate. During this visit, the National Institute of Biomedical Imaging and Bioengineering also showcased its AI initiatives. Dr. Rutter underscored having AI/ML at the forefront of biomedicine and the importance of transparency and data capture as NCATS communicates to the Senate and other congressional members about this topic. On September 11, 2024, Dr. Rutter shared updates on N3C with Rep. Diana L. DeGette (D-Colorado) and her staff. She also heard Rep. DeGette's ideas about the 21st Century Cures Act 2.0 and her motivation for interest in rare disease research and connection to NCATS CAN Review Board.

- **Rare Disease Therapy Development Meeting.** NIH, Centers for Medicare & Medicaid Services, and FDA leadership gathered at the FDA White Oak Campus for a joint meeting on rare disease therapy development. The purpose of the meeting was to understand how these agencies can better coordinate efforts related to rare diseases. They discussed expanding rare disease priorities at NIH to enhance interagency coordination. The meeting addressed a variety of topics, including putting patients and families at the center and conducting natural history studies. When the workshop ended, participants refined the topics and began sorting them into priority areas likely to be productive over the next few years.

- **NCATS–FDA Translational Science Interagency Fellowship.** NCATS and the FDA began this jointly sponsored fellowship in 2021 and inducted the first class of fellows that year. In this program, fellows perform 18-month rotations with both the FDA and NCATS, which need not be consecutive. The aim is to cross-train scientists in both regulatory science and translational science. The expectation is that fellows will use their experience and training to acquire related positions in the workforce. This interagency fellowship remains one of NCATS' premier programs. Three fellows graduated the program in September 2024 and have accepted positions in industry and the government: Elia Lopez, Ph.D., lead scientist, Oligonucleotides, Vial, Inc.; Xinh-Xinh Nguyen, Ph.D., staff fellow, FDA; and Keyla Tumas, Ph.D., CURE ID project manager, NCATS.

NCATS Program Updates

Dr. Rutter provided an update on NCATS programs and highlighted a Clinical and Translational Science Awards (CTSA) Program to screen newborns.

- **Newborn Screening by Whole-Genome Sequencing (NBSxWGS).** The CTSA Program and the NIH Common Fund (CF) launched the NBSxWGS program as a CF Venture Space Initiative. This program was conceptualized in DRDRI, and Phillip John (P.J.) Brooks, Ph.D., deputy director, DRDRI, will lead this program for NIH, partnering with the *Eunice Kennedy Shriver* National Institute of Child Health and Development and Diana Bianchi, Ph.D., and her team. The objective is to demonstrate the feasibility of a collaborative model for NBSxWGS through state public health laboratories and a centralized sequencing laboratory. NBSxWGS will be a $5 million annual investment extending over 3 years and will consist of a small-scale demonstration project conducted across multiple states to show potential for a national program. Projects demonstrating the feasibility of a national program would be an important advance for more equitable access and for keeping pace with therapeutic developments for rare diseases. She noted that many people with rare diseases have a long diagnostic odyssey. Newborn screening may be able to shorten that diagnostic odyssey and likely allow starting treatment sooner.

- **Accelerating Medicines Partnership® (AMP) Bespoke Gene Therapy Consortium (BGTC).** NCATS, the FDA Center for Biologics Evaluation and Research, and the Foundation for the NIH (FNIH) established the BGTC, a major component of the FNIH Gene Therapy AMP. This public–private partnership consists of 11 NIH institutes and centers (ICs); the FDA; and multiple pharmaceutical and life sciences companies, nonprofits, and other organizations. Through the BGTC, eight rare diseases have been selected for gene therapy and manufacturing pairs for clinical trials. NIH will advance six of the eight gene therapies. In support of the BGTC, the NCATS Therapeutic Development Branch has received three Orphan Drug Designations (ODDs) and six Rare Pediatric Disease Designations (RPDDs) from the FDA for various rare disease treatments. Dr. Rutter noted the importance of demonstrating that the prevalence data are indicative that these are rare diseases. A drug that is approved through a RPDD is eligible for a priority review voucher. Congress recently passed the priority review voucher, which allows these vouchers to be sold for prices that exceed $100 million dollars. Similarly, the ODD provides incentives to encourage the development of treatments for rare diseases. These incentives include 7 years of market exclusivity, tax credits, and waiver of FDA fees. These benefits for developing these treatments are tangible, and this level of success gives NCATS even more confidence and excitement to move forward in the BGTC space. Dr. Rutter acknowledged NCATS and FDA partners for their efforts in advancing this field.

- **Metformin Target Trial Emulation Using the National COVID Cohort Collaborative (N3C).** The Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV)-6 clinical trial consists of seven arms, which have been completed on time, under budget, and with the targeted enrollment. The final clinical trial — the metformin arm of ACTIV-6 — opened for enrollment in July 2023 and evaluated the final of five drugs during the 5-year study. This phase of the ACTIV-6 trial also evaluated a primary endpoint of time to recovery from acute symptoms, with a 6-month follow-up. The Early Outpatient Treatment for SARS-CoV-2 Infection (COVID-19) trial (COVID-OUT), which was completed before this study, suggested that using metformin might prevent long COVID. This phase of the ACTIV-6 trial is being managed for NCATS by Sarah E. Dunsmore, Ph.D., program director, Office of Translational Medicine; it evaluated a primary endpoint of time to recovery from acute symptoms, with a 6-month follow-up. ACTIV-6 has

enrolled nearly 1,800 participants since the trial opened, and the goal is to perform evaluation and follow-up with 3,000 participants. Data from ACTIV-6, which is examining metformin in a randomized trial, combined with real-world metformin usage data collected under similar conditions through the N3C Public Health Answers to Speed Tractable Results (PHASTR) program, formed and tested a use case for trial emulation methodology. NCATS launched PHASTR in 2023 to extract from the N3C Data Enclave electronic health record data of outpatients who started taking metformin after a positive COVID-19 test. Results will be presented at the Infectious Diseases joint annual meeting, IDWeek, in October 2024, and a randomized clinical is being planned. Information about the Metformin Target Trial Emulation Using N3C Data Enclave and PHASTR, as well as validation of COVID-OUT results, can be accessed through the N3C Dashboard.

NIH Community Engagement: Incorporating Public Voices in Clinical Research

Dr. Rutter explained that NIH initiated the Novel and Exceptional Technology and Research Advisory Committee (NExTRAC) in 2023. NExTRAC addresses specific projects regarding community engagement. Dr. Rutter highlighted examples of such projects and NIH's community engagement efforts to incorporate public voices in all aspects of clinical research.

- **NIH Engaging the Public as Partners in Clinical Research (ENGAGE) Working Group.** Recognizing that engaging communities requires different approaches, NIH leveraged NExTRAC and launched ENGAGE and the ENGAGE Working Group to ensure that NIH is maturing in this space, particularly in the area of community engagement partnerships. Dr. Rutter works with a team across NIH on this initiative.

- **ENGAGE Case Studies.** NIH has established an NIH-wide group to develop case studies, which are then used as a resource for the broader NIH community. The aim is to understand the best practices in the realm of community engagement and what approaches have been used. Detailed information can be accessed from the ENGAGE webpage. Dr. Rutter highlighted a few case studies. DRDRI has a Tool Kit for Patient-Focused Therapy Development that helps patients find researchers interested in their rare disease. The Faster Together online course is a CTSA Trial Innovations Network–supported resource designed to help researchers understand how they can ensure that minority populations participate in clinical trials. The NIH Community Engagement Alliance (commonly called CEAL) partners with communities to improve health. Dr. Rutter co-authored a post for the *Under the Poliscope* blog with Lyric Jorgenson, Ph.D., NIH associate director for science policy, to highlight these use cases. She encouraged the Council members to look at these use cases, which are updated frequently.

- **Communities Advancing Research Equity for Health™ (CARE for Health™).** In June 2024, NIH announced the CARE for Health™ program, which had been approved by the NIH Council of Councils in April 2024. This initiative is a key priority for NIH Director Dr. Monica M. Bertagnolli and aims to develop Network Research Hubs to reach more of the primary care settings and leverage the clinical strengths within NIH. Participant and community engagement is a key pillar of this program that strives to innovate clinical trial designs to incorporate primary care in communities. The co-chairs of this program are Dr. Rutter; Helene Langevin, M.D., director, National Center for Complementary and Integrative Health; and Debara Tucci, M.D., M.S., M.B.A., director, National Institute on Deafness and Other Communication Disorders. Michael G. Kurilla, M.D., Ph.D., director, Division of Clinical Innovations (DCI), NCATS, is on the steering committee. The first awards will be announced soon.

NCATS Strategic Plan 2025–2030

Dr. Rutter reported that the *NCATS Strategic Plan for 2025–2030* has been released. She briefly noted the strategic planning process and expressed appreciation to the strategic planning team — Meredith D. Temple-O'Connor, Ph.D., M.S., chief, Policy Branch, Office of Policy, Communications and Education (OPCE), OPCE Policy Branch staff; Jessica C. Walrath, Ph.D.; and Jennifer M. Beierlein, Ph.D. — for their tremendous effort in organizing and coordinating this process. She also acknowledged NCATS constituents (internal and external), who have been engaged from the beginning, and NCATS staff for their support. The strategic plan encompasses NCATS' vision (more treatments for all people more quickly) and includes in five goals:

- Goal 1: Advance development of and access to more treatments, particularly for diseases with unmet needs.
- Goal 2: Empower everyone to contribute to and benefit from translational science.
- Goal 3: Accelerate translational science by breaking barriers and boosting efficiency.
- Goal 4: Leverage crosscutting strategies to enhance translational science.
- Goal 5: Champion effective stewardship of translational science through transparency, integrity, accountability, and social responsibility.

Dr. Rutter highlighted that the next steps include hosting an NCATS Director Roundtable Series, "Translating the Strategic Plan into Action," to discuss how the community can begin implementing the plan.

Summary

Dr. Rutter summarized that NCATS leadership is in place, FY25 budget approval is pending, and a CR to fund the government is likely. She noted congressional briefings with NCATS and the interagency commitment to rare diseases. She highlighted impactful advances, including the CF's implementing Venture Initiative NBSxWGS, ACTIV-6's completing enrollments for all phase 3 studies, BGTC's RPDD being granted by the FDA, and the launching of both the ENGAGE initiative and CARE for Health. She provided an update on the *NCATS Strategic Plan for 2025–2030*. The Council will hear program updates from the Office of the Director, DCI, DPI, and Office of Drug Development Partnership Programs. After the summary, Dr. Rutter introduced Council's inquiry for institute process initiation letter.

NCATS Advisory Council Inquiry for Institute Process Initiation

Dr. Rutter called attention to the formal written request of the Council to initiate the process of a transition of NCATS to an institute. This letter has been signed by current and past Council members. Dr. Rutter expressed her gratitude for the robust response and thoughtfulness of the Council members, in which they present compelling arguments based on precedent for NCATS' becoming an NIH institute. Similar processes have resulted in other ICs' being elevated from centers to institutes, including the National Human Genome Research Institute, National Institute on Minority Health and Health Disparities, and National Institute of Nursing Research. Dr. Rutter remarked on the honor of leading NCATS as an institute to accomplish even more advances and quoted excerpts of the Council's request. She invited Council members to share any additional comments or questions.

On behalf of the Council, Ms. Kennedy commented on NCATS' achievements, comprehensive strategic plan, unparalleled leadership, and robust translational research portfolio. She underscored how implementation of NCATS' mission going forward would best be achieved by NCATS' being elevated from a center to an institute. This status will ensure that NCATS remains at the forefront of science and continues NIH-wide collaborations, spurs biotechnology innovation, and expands the drug development

landscape for rare disease research innovation. Ms. Kennedy remarked that conducting trials beyond phase 2B clinical trials would boost NCATS' future and unlock its full capacity to deliver more treatments for all people more quickly.

VI. SPECIAL TOPIC PRESENTATIONS AND DISCUSSION

Pathways to Inclusion: Transforming Leadership, Strategy, and Science for Equity: Jeanita S. Pritchett Clay, Ph.D., Chief Scientific Diversity Officer (CSDO), Office of the Director (OD), NCATS

Jeanita S. Pritchett Clay, Ph.D., described strategic initiatives for cultivating a diverse workforce, fostering inclusive leadership, and integrating equity in health research. She discussed developing an impactful diversity, equity, inclusion, and accessibility (DEIA) program. NCATS recently published eight translational science principles, which align with the *NCATS Strategic Plan* and provide a guide to approaches for overcoming long-standing challenges along the translational science research pipeline. Themes include team science, boundary crossing, partnerships, crosscutting solutions, and DEIA, on which Dr. Pritchett Clay focused her presentation. As NCATS' inaugural CSDO, her main role is to harmonize, elevate, and align various DEIA efforts across NCATS, as well as NIH. To achieve this, Dr. Pritchett Clay serves as a thought partner in connecting with NCATS divisions and offices, brainstorming ways to integrate various principles into their work streams and leveraging data to help inform the different DEIA initiatives. She also assists in promoting community outreach and engagement and partnerships and collaboration to address potential workforce needs.

Bright Inclusion, Diversity, Equity, and Accessibility Strategies (IDEAS) in Action

Dr. Pritchett Clay highlighted strategies implemented across NCATS, showing their intersection with DEIA. Bright IDEAS encompass various activities that include outreach and engagement, as well as recruitment and retention efforts for attaining, growing, and developing staff into leaders of the future. Efforts will focus on exploring different staff-led organizations and their impact on shaping NCATS culture. In the NCATS research portfolio, health equity and health disparities research will be emphasized. Another focus will be on engaging patient advocacy groups.

Dr. Pritchett Clay described examples of DEIA strategies across NCATS.

- **Strategic Recruitment, Community Engagement, and Outreach.** To spur interest in translational science and NCATS' mission, Dr. Pritchett Clay and her team connect with the future biomedical workforce at scientific conferences and national meetings. Activities include distributing informational flyers, conducting interactive sessions to discuss NCATS' research, and helping build capacity in ways interested parties can engage with NCATS. The team supports researchers visiting their communities to describe their research. The aims are to visit untapped areas of limited resources and diversity in research and to ensure that NCATS is positioned as a model employer for future employees. Recent engagements included recruitment activities at the D.C. Pride Festival, National Urban League Business Executive Exchange Program Empowerment Summit, Central Intercollegiate Athletic Association career fair, Gallaudet University Career Day, and American Chemical Society Diversity Leaders' Summit. The NCATS OD also started a K–12 outreach and engagement program, focusing on early engagement with the next generation to educate and excite them about translational science, team science, and collaboration with one another.
- **Demographic Data and Recruitment Toolkit.** NCATS reviews its NIH workforce demographic and recruitment data to measure its progress in workforce diversity. Data are stratified by race, ethnicity, sex, and disability and are updated periodically by the NIH Office of Equity, Diversity,

and Inclusion (EDI). These data, coupled with information from surveys and focus groups, provide NCATS with a more detailed review of the status and what to address in future DEIA activities. Dr. Pritchett Clay and her team are working with NCATS staff to develop a recruitment and hiring toolkit to aid in ensuring that NCATS is incorporating equity throughout its processes. Furthermore, NCATS has added questions focused on DEIA to employee exit interviews.

- **Learning Opportunities, DEIA-Related Seminars, and Resources.** Dr. Pritchett Clay highlighted opportunities and seminars that have been provided for NCATS staff, leveraging feedback from the Federal Employee Viewpoint Survey regarding potential opportunity areas for growth. NCATS partnered with institutes and centers to host Train-the-Trainer workshops on microaggressions to help staff to comfortably identify microaggressions and trained staff to teach on this topic. NCATS partnered with NIH EDI to sponsor accessibility seminars. This series explored accessibility to help staff better understand how to implement compliance with Section 508 of the Rehabilitation Act in their work products. Discussions also focused on digital accessibility. Last, NCATS has laid the groundwork in hosting a DEIA seminar series and providing resources on assisting staff in understanding systemic barriers. These barriers have challenged staff growth and impeded their becoming more engaged employees.

NCATS Staff-Led Groups: Shaping Diversity, Equity, Inclusion, and Accessibility

Dr. Pritchett Clay noted that staff-led groups have helped to shape DEIA in NCATS. She highlighted four of those groups.

- **Inclusion, Diversity, Equity, and Accessibility Council.** This Council, composed of NCATS-wide representation, implements initiatives to advance DEIA through working groups.
- **Employee Engagement Committee.** Promotes a positive work–life culture and advises on issues related to work–life enrichment activities that influence the morale and well-being of all staff. Activities include the NCATS social group, book clubs, and seminars.
- **NCATS Women Scientist Advisors.** A group of women scientists and allies that focuses on raising awareness of issues facing women scientists and improving women's representation among NIH faculty at all levels.
- **NCATS Executive and Staff Assistant Committee.** Provides an inclusive workplace where committee members can attain optimal performance by sharing constructive feedback and collaborating on solutions.

Diversity, Equity, Inclusion, and Accessibility in Translational Science and Health Research

Dr. Pritchett Clay informed the Council of NCATS' contributions to the literature, demonstrating that NCATS is approaching DEIA from many angles. Several staff members have published journal articles and opinion pieces emphasizing the importance of DEIA in translational science. In 2022, the NCATS Office of Policy, Communications and Education, Education Branch (Hussain SF, et al.) reported in the *Journal of Clinical and Translational Science* on perspectives from NCATS about DEIA as essential to advance the goals of translational science. The authors highlighted several strategies for integrating DEIA into the translational science spectrum. In 2023, NCATS Division of Rare Diseases Research Innovation (Brooks PJ, et al.) authored an article in *Medpage Today* offering a closer look at the approval of CRISPR/Cas9 gene therapy for sickle cell disease. The authors explored sickle cell disease and outlined some of the historical considerations and implications around that disease for future diseases.

NCATS Ongoing Diversity, Equity, Inclusion, and Accessibility Journey

Dr. Pritchett Clay emphasized the importance of leveraging the output of the *NCATS Strategic Plan* to be sustainable in DEIA and using it as a launching pad for future directions. During the past year, Dr. Pritchett Clay and her team have been gathering information, exploring different data sources, and empowering NCATS leaders and supervisors to be equipped in DEIA. She described NCATS' organizational culture and impact roadmap. NCATS is positioned to develop a roadmap that will outline ongoing DEIA activities that focus on organizational culture and impact. This roadmap, one of the early outputs of the strategic plan, outlines key pillars, objectives, strategies, and actions that can be used during the implementation phase of the DEIA actions. NCATS' DEIA journey began with a landscape assessment and gap analysis, during which Dr. Pritchett Clay gathered copious data from a variety of sources and met with staff in DEIA dialogue sessions. NCATS DEIA activities informed four proposed pillars for a roadmap that aligns with NCATS' vision of more treatments for all people more quickly.

- Pillar 1: Cultivate a diverse, inclusive, and representative workforce to achieve the NCATS mission.
- Pillar 2: Foster a safe and welcoming NCATS culture to promote a sense of belonging and growth within the organization.
- Pillar 3: Invest in and support research areas and initiatives that reduce health inequities and address health disparities.
- Pillar 4: Leverage NCATS' resources, funding opportunities, and databases to engage communities, raise awareness, and support innovation across the translational science spectrum.

Dr. Pritchett Clay noted that NCATS anticipates releasing this DEIA culture and impact roadmap along with objectives by the end of the first quarter of FY25. She next highlighted other interrelated NCATS initiatives, including core values that align with the strategic plan and a racial and ethnicity equity plan that has been in development during the past 2 years. NCATS' key initiatives support and enable its goal to innovate, collaborate, and transform the way research is done, making it faster, more efficient, and more impactful. Dr. Pritchett Clay summarized that the core values include diversity, equity, inclusion, accessibility, and belonging, which is integral and necessary for NCATS to achieve its bold and audacious goals. She touched on how DEIA in an organization leads to community belonging, which encompasses several components, including leading by example.

Efforts to Advance Equity in Preclinical Research and Therapeutic Development: Sharie J. Haugabook, Ph.D., Acting Head, Scientific Project Management, Therapeutic Development Branch (TDB), Division of Preclinical Innovation (DPI), NCATS

Sharie J. Haugabook, Ph.D., described a general concept of equity from a biomedical research perspective. She provided a broad overview of where therapeutic drug development sits in the biomedical research enterprise and discussed why advancing equity in research is important. Unlike equality, equity recognizes that each person has different circumstances and then allocates the specific resources they need to have an equal outcome. Advancing equity leads to justice. In the biomedical context, equity is assessed by research capacity, access to funding, prestige and privilege, and open science practices. The threshold for research comes with a lack of transparency, which impedes equitably correcting a deficit and changing the distribution of the resources.

Equity and disparities in biomedical research usually focus on interactions with more patients or where research participation occurs (e.g., health care delivery and clinical research). Advancing equity extends to the basic, preclinical, and translational spaces. Identifying opportunities along and within that part of

the therapeutic development pipeline to position and implement equity-focused strategies is critical. DPI conducts research in the boundary between health care delivery and clinical research.

Dr. Haugabook described an approach to advancing equity in preclinical research and therapeutic development. DPI engaged the Health Federally Funded Research and Development Center (FFRDC) operated by Mitre to develop an approach for infusing equity into the preclinical therapeutic development space, utilizing rare diseases as an exemplar. The approach consisted of five steps: (1) develop an action plan, (2) explore that action further through an environmental scan, (3) apply a critical equity lens to the points of engagement in the DPI TDB, (4) disseminate the findings, and (5) implement the recommendations. In an iterative process of engaging, revising, and learning through steps 3 through 5, Health FFRDC generated several findings, which were developed first into recommendations and then into three major actions, which Dr. Haugabook described.

Action 1: Applying an Equity Lens to the Evaluation Process for New Project Collaborations

Dr. Haugabook explained that the finding for this action was that diseases affecting underserved populations struggle to find the resources or institutional support for preclinical development. The recommendation was to augment the evaluation and decision-making process for new project selection to explicitly account for equity. Regarding the proposal and evaluation, the aims were to identify all known populations affected by a disease in the target product profile; identify which populations might benefit from the proposed treatment; and request aggregate de-identified demographic information for data presented and derived from patient samples. Collaborative opportunities included identifying drug candidates from lead optimization through late FDA Investigational New Drug (IND)–enabling studies and requiring catalytic engagement to fulfill critical development gaps and to advance translation. For portfolio balancing, the goals were to diversify efforts and treatment modalities toward a balanced portfolio and to include platform therapies, N = 1 therapies, and repurposed or repositioned molecules.

- **Preclinical Equity Index (PEI) Concept Tool.** NCATS is disease agnostic, presenting both a challenge and an opportunity. Approximately 10,000 rare diseases are known, and many others are yet to be identified. A remaining question is how to achieve a more consistent and complete picture of the disease landscape and explicitly account for equity beyond evaluated scientific dimensions to address that landscape. DPI conceptualized an approach with Mitre to develop a PEI to complement the evaluation process. The PEI is an interactive application that introduces new criteria focused on equity presented in a yes–no binary questionnaire. The PEI produces quantitative scoring of each disease visualization across different categorical dimensions to enable TDB to evaluate equity profiles from the screenshots. The output is the questionnaire that is answered. Users can input their data on cumulative research funding to produce another visualization. Users also can input funding information through the NIH RePORTER.

Action 2: Engaging the Community

Dr. Haugabook noted the finding that limited engagement with patients and disease communities can obscure their top priorities from research institutions. The recommendation is to sustain and expand community engagement to ensure research efforts are informed and focus on patients' top priorities and unmet needs.

- **Seminar Series.** In 2023, NCATS established a seminar series on rare diseases inclusive of more researchers' voices and the patients, advocates, physicians, and other partners of interest. A conversation format was adopted over a lecture, and the series continues to evolve, incorporating the speakers' preferences and diverse perspectives from community members on what equity means to them. Videos can be accessed on the NCATS YouTube channel.

Action 3: Sharing Knowledge

Dr. Haugabook explained that patients, communities, and advocates frequently navigate their diseases on their own, becoming their own researcher, advisor, data expert, sample collector, and knowledge broker. One recommendation is to expand investments in developing scientific foundational knowledge but also promote easier access to this knowledge for rare diseases.

- **RARe-SOURCE™ for Preclinical Research.** The NCATS TDB is developing RARe-SOURCE™ as a bioinformatics platform for rare diseases. One module focuses on the basic, preclinical, and scientific research and bringing data together to make connections among diseases, phenotypes, associated variants, genes, proteins, and pathways and related chemistries. These connections provide new insight on commonalities among disorders that could point to common mechanisms and approaches to platform therapy development. In the AI literature module, users can access published, peer-reviewed information on rare diseases using an algorithm-based search to extract data.

Dr. Haugabook also noted that research partners and advocates are unfamiliar with the specifics of preclinical phase activities and requirements after the initial drug discovery work. The recommendation is to develop and disseminate educational resources that introduce the preclinical phase and explain the detailed requirements of a successful drug candidate.

- **Knowledge Guide for Preclinical Research and Development**. The NCATS TDB, in collaboration with Mitre, has developed a Knowledge Guide that focuses on the specific scientific activities of preclinical drug development, from candidate selection to IND-enabling studies. This tool is still being developed and refined. Participants can subscribe to the NCATS Newsletter for updates on a release date.

Discussion

Paul A. Harris, Ph.D., asked about the use of the PEI to inform next steps. Dr. Haugabook explained that the purpose of the tool is to understand the disease landscape and that proposals are not being compared to one another. The aim is to avoid duplication of funding. NCATS is disease agnostic and is focusing on the resources and understanding the durability aspects of whether specific targets are ready for an investment. She confirmed that proposals are submitted to the TDB and could be extended to other programs. Joni L. Rutter, Ph.D., commented on having the ability and resources to produce graphs of diseases that are not being studied for various reasons and increasing that knowledge. Although the current capacity is limited, the plans are to grow and refine the tool over time and expand research. Matthew D. Hall, Ph.D., added that this tool can help identify understudied areas for potential investment.

VII. PROGRAM UPDATE PRESENTATION AND DISCUSSION: Division of Clinical Innovation (DCI): Michael G. Kurilla, M.D., Ph.D., Director, DCI, NCATS

Michael G. Kurilla, M.D., Ph.D., provided an update on DCI activities and focused on the state of the Clinical and Translational Science Awards (CTSA) Program. Under the new UM1 program, 11 CTSAs were awarded in FY24, two of which are new.

Division of Clinical Innovation Staff Updates

Dr. Kurilla presented a summary of staff updates for FY24; new staff include Anthony T. DiBello, Ph.D., program director, Education and Training Section, CTSA Program Branch; Irina N. Krasnova, Ph.D.,

program director, Education and Training Section, CTSA Program Branch; and Karina K. Salazar, M.D., Ph.D., senior clinical research advisor, Clinical Research Resource, Clinical Affairs Branch, Trial Innovation Network. He announced that Heather L. Baker, health science policy analyst, was promoted to senior program coordinator, Office of the Director. Dr. Kurilla remarked that these staff will help facilitate increased coordination and harmonization of activities across DCI.

Recognitions and Awards

Dr. Kurilla highlighted recent accomplishments by CTSA investigators, scholars, and trainees.

- **Investigator Awards.** Julie A. Bastarache, M.D., was elected vice president of the American Society for Clinical Investigation for 2024–2025; then she will serve as president-elect for 1 year and as president of the society in 2026–2027. Rhonda D. Szczesniak, Ph.D., received the Cystic Fibrosis Foundation's Clinical Research Award. Vesna D. Garovic, M.D., Ph.D., received the American Society of Nephrology Barbara T. Murphy Award, and she will deliver the Arthur C. Corcoran Memorial Lecture at the American Heart Association's Hypertension Scientific Session. Nicole C. Woitowich, Ph.D., received the American Society for Biochemistry and Molecular Biology Emerging Leadership Award. Terrence Tsou, M.D., M.P.H. candidate and TL1 trainee, received the 2024 Alliance for Clinical and Translational Science Outstanding Trainee Predoctoral Scholar Award.

- **National Recognition for Innovation Faculty Position.** Eric Topol, M.D., Scripps Research Translational Institute, was named among the inaugural TIME 100 Health (100 most influential people in health) and received the Friends of the National Library of Medicine's Donald A.B. Lindberg Distinguished Health Communications Award. David Huang, M.D., Ph.D., Oregon Health & Science University, Oregon Clinical and Translational Research Institute, received the 2024 Oregon History Maker Award from the Oregon Historical Society, the 2023 National Medal of Technology and Innovation, and the 2023 Lasker-DeBakey Clinical Medical Research Award. Dr. Huang was recognized for his seminal article on optical coherence tomography, published in *Science* in 1991, and has been cited more than 18,000 times. In addition, he helped pioneer new applications of this groundbreaking technology that transformed the way eye disease is diagnosed and managed.

- **National Recognition for Advancing Health Equity**. Elizabeth O. Ofili, M.D., M.P.H., FACC, professor of medicine, director and senior associate dean, Clinical Research Center and Clinical and Translational Research, Morehouse School of Medicine, was invited in June 2024 to the White House Clinical Trials Forum, which was organized by the White House Office of Science and Technology Policy to highlight pressing issues in clinical trials and innovative approaches to making clinical trials more inclusive and accessible to all Americans. Dr. Ofili was recognized for her role in developing Health 360x, a mobile and web-based participant registry with culturally congruent coaching.

Clinical and Translational Research Awards Program Consortium Activities (FY24)

Dr. Kurilla summarized current R03 awards, which are intended to support K scholars. The current awardees reflect a broad research portfolio, including the impact of high-deductible health plan enrollment on health spending and utilization and comparisons by income.

Clinical and Translational Research Awards Collaborative Innovation Awards (CCIA*)*

- **Bytes to Bedside: Collaborative Development for Translational Clinical Decision Support.** Six CTSAs are addressing the problem that existing models of operations and research involving Electronic Health Records (EHR)-based clinical decision support (CDS) systems are institution specific, not tied to clinical outcomes, and not scalable. This project aims to develop, demonstrate, disseminate, and evaluate a centralized and highly efficient data-sharing infrastructure to support translational CDS analysis and benchmarking of performance across six collaborating institutions.

- **Improving Efficiency, Quality, and Equity: Randomized Controlled Evaluations of Remote Versus In-Person Clinical Trial Methods.** Five CTSAs are proposing an innovative, rigorous experimental evaluation of remote versus in-person methods for trial efficiency and quality across three randomized control trials (for smoking cessation, a mobile health intervention for depression, and an opioid overdose education and naloxone intervention). This study examines the impact of remote versus in-person trial efficiency and quality for participant subgroups that experience health inequities.

Clinical and Translational Research Awards Program Impact

- **Precision Medicine in the Diagnosis of Genetic Disorders in Neonates.** A CTSA pilot award was granted in 2018 to evaluate rapid whole genome sequencing and a targeted neonatal gene panel in infants with a suspected genetic disorder. This has been the largest study in the field, enrolling 400 patients and comparing whole genome sequencing to panel analysis. The results revealed an abnormality in 49 percent of patients, and 19 percent changed care. Follow-up analysis examining cost savings through the first year showed $150,000 in savings in health care costs. A smaller effort will focus on the 51 percent who had no identified abnormality.

National COVID Cohort Collaborative Transitioning to National Clinical Cohort Collaborative (N3C)

Dr. Kurilla noted that NCATS is transitioning from the National COVID Cohort Collaborative to the National Clinical Cohort Collaborative (N3C). N3C was originally conceptualized with a 5-year data transfer agreement. Individual institutions supplying data can choose to re-enlist for another 5 years. N3C COVID remains open. Three pilot studies are in progress with this transition: Data Science Enclave, Pilot Renal Enclave, and Pilot Cancer Enclave. Dr. Kurilla highlighted one of the three. The Data Science Enclave is a collaboration with NCATS and the NIH Office of Data Science Strategy to establish an educational resource for data science to teach, develop, and share educational material on data science. The data source will be synthetic data sets (Level I). Dr. Kurilla remarked on how these pilots will provide NCATS with the critical evaluation to understand the requirements for the infrastructure needed to support this work, as well as the resources that institutions need to take advantage of it.

National ENACT Network

Evolve to Next-Gen ACT (ENACT) is a federated system. More than 50 CTSAs are participating, utilizing more than 140 million patient EHRs. The intent is to make ENACT more practical for individual clinicians, so those who do not have advanced degrees in data science or informatics can take advantage of this resource. ENACT is aiming to be more user accessible in terms of clinical decision-making capability.

Pain Management Effectiveness Research Network (ERN)

Four ERN clinical trials are fully enrolled and test pain conditions and interventions — including musculoskeletal, acute, and chronic pain. Some trials experienced delays due to COVID-19 and staffing

challenges. The ERN trials in the implementation phase that are receiving full resource center support have achieved 98 percent of their overall recruitment goal and are on track for completion. Other trials receiving resources but not involving the full ERN had successful completion rates. Because of the achievements of this program in NCATS and NIH-wide, a funding recompetition is being considered.

Administrative Supplements

Dr. Kurilla remarked that the CTSA Program receives co-funding from several ICs for training programs and various research topics, including Down syndrome.

Clinical and Translational Research Awards Program News

- **Monocyte Transcriptomic Profile Following Eicosapentaenoic Acid (EPA) and Docosahexaenoic Acid (DHA) Supplementation.** The U.S. Department of Agriculture engaged the resources of Tufts University Clinical and Translational Science Institute to further evaluate the differences in the effects in cardiovascular disease in men and women following EPA and DHA supplements.

- **Investigating Microplastics in Human Tissue.** University of New Mexico Health Sciences CTSA investigators developed an assay to measure the quantity of micro- and nano-plastics.

- **ChromoSeq: Clinical, Community, and Economic Impact.** Researchers at the Washington University School of Medicine in St. Louis CTSA developed ChromoSeq, a diagnostic test, for two types of blood cancers: myelodysplastic syndromes (MDS) and acute myeloid leukemia (AML). In August 2023, ChromoSeq became the first whole genome sequencing test for cancer to be approved for reimbursement by Centers for Medicare and Medicaid (CMS).

- **Validation of Trial of Labor After Cesarean Delivery Risk Calculator.** In 2022, the National Institute of Child Health and Human Development (NICHD) released a modified calculator, called the Trial of Labor After Cesarean (TOLAC) calculator, that removed race as a variable. The University of California (UC), Davis, CTSA collaborated with NICHD to externally validate the TOLAC calculator using UC Davis' data sets. The results revealed that TOLAC predicted risk after a Cesarean section, which resulted in improved health for Black and Hispanic women. TOLAC is being adopted and used at other institutions.

- **Building Trust and Finding Trustworthiness.** The University of Kentucky Center for Clinical and Translational Science CTSA is leveraging the history of Black churches as a trusted center for community support and empowerment to promote colorectal cancer screening activities and reducing disparities.

Clinical and Translational Research Awards Researcher Spotlight

Dr. Kurilla highlighted rising leaders within the CTSA Program.

- **Institutional Mentored Career Development Award (KL2) Scholars.** Chidiogo Anyigbo, M.D., M.P.H., was named one of Emory University's 40 Under 40 Notable Alumni and was selected for the *Cincinnati Business Courier's* 40 Under 40 class. Dr. Anyigbo is a current KL2 Scholar at the Cincinnati Center for Clinical and Translational Science and Training. Her research focuses on the first 4 months of life, food insecurity, health-related social issues associated with adverse infant behavioral functioning at 6 months, and early household interventions.

- **Former Institutional Mentored Career Development Award (KL2) Scholars.** Gunisha Kaur, M.D., M.A., is associate professor of anesthesiology, director, Human Rights Impact Lab, medical

director, Weill Cornell Center for Human Rights, Weill Cornell Medicine. She was selected as an Emerging Leader in Health and Medicine Scholar by the National Academy of Medicine in 2023 and received a 2023 National Academy of Medicine Healthy Longevity Award. Her research focuses on digital solutions to reduce maternal morbidity and mortality in refugee women. Allison Webel, Ph.D., RN, FAAN, is co-chair, International HIV/AIDS Nursing Research Network, associate dean of research and professor of Child, Family and Population Health Nursing, University of Washington School of Nursing. Her research focuses on strategies to improve symptom management and healthy aging in adults living with HIV, and her laboratory coordinates the Impact of Physical Activity Routines and Dietary Intake on the Longitudinal Symptom Experience of People Living with HIV study.

- **Clinical Research Training Awards (TL1) Trainees.** Carly Herbert, M.D., Ph.D. candidate, was first author of a report of an NIH-funded Rapid Acceleration of Diagnostics (RADx), commonly referred to as RADx, study evaluating the different viral dynamics during acute SARS-CoV-2 infection by sex and body mass index.

- **Diversity/Reentry Supplement Awards.** Six awards were made in FY24. Dr. Kurilla highlighted the work of two of the six awardees. Suelen Lucio Boschen De Souza, Ph.D., is studying Parkinson's disease and deep brain stimulation. DaShaunda Taylor, Ph.D., M.P.H., is advancing health equity for pregnant women and new mothers with substance use disorder.

Using EHRs to Identify a Rare Disease

Dr. Kurilla described his review of studies using EHRs to identify acute hepatic porphyria (AHP). AHP is a group of rare but treatable conditions associated with diagnostic delays averaging 15 years. A 2024 report on reducing this delay by using EHR data and machine learning (ML) investigated improving the diagnosis of disease. The study showed that the ML algorithm identified 71 percent of cases 1.2 years earlier than had been reported. Dr. Kurilla highlighted that the co-lead author on this study was Katharina Schmolly, M.D., who conducted her research at the UCLA clinical and translational science institute (CTSI) as a TL1 summer fellow. She graduated with her M.D. in May 2024 and is currently an internal medicine resident at the Geisel School of Medicine at Dartmouth. Dr. Schmolly and her colleagues have launched the website ZebraMD, dedicated to improving diagnosis, management, and research in rare and genetic diseases, emphasizing her ambition and goal of using EHRs to identify unrecognized and undiagnosed rare diseases.

Training the Next Generation of Cutting-Edge Physician Scientists

Dr. Kurilla noted that NCATS is congressionally mandated to train the next generation of cutting-edge physician–scientists. The University of Pennsylvania's Institute for Translational Medicine and Therapeutics (ITMAT) has an undergraduate Translational Research Immersion Program (TRIP), which is a 10-week mentored summer research program. A survey of the participants completing the program showed that 23 had continued to graduate school programs, 50 percent of which were M.D. programs. Dr. Kurilla highlighted two former TRIP students — Jackson Milone at Franklin & Marshall College and Sarah Ramirez at Bryn Mawr College — who were part of research teams that published the results of two studies. One study investigated gene and environment effects and mediation involving adverse childhood events, mood and anxiety disorders, and substance dependence. The second study evaluated the application of polygenic scores to a deeply phenotyped sample enriched for substance use disorders.

Dr. Kurilla remarked that the ITMAT TRIP provides undergraduate and graduate students with the opportunity to conduct research and noted the need to sponsor research experiences that train youth

during the early school years. The New York University (NYU) Langone CTSI CTSA sponsored such an activity connected with a CTSI CTSA pilot award. NYU Grossman School of Medicine students and then-high school students, Heewon Alexandra Moon and Jacob R. Blaustein, were first authors on a recent publication investigating indoor particulate air pollution in residences in historically redlined districts in the New York City area. This and other CTSA activities have shown that 2.5-micron-diameter particulate matter is associated with cardiovascular and pulmonary problems later in life and can be addressed by improving basic indoor and outdoor cleaning where people live.

2020s Version of Video Games

Dr. Kurilla explained how video games are moving into a new era — from predominant use by youth to military use with unmanned drones, for example. He highlighted that Anu Iyer, a pre-med student at the Georgia Institute of Technology, has been designing deep-learning models with the University of Arkansas for Medical Sciences (UAMS) Translational Research Institute (TRI) CTSA since she was 14 years old. Ms. Iyer is first author on a UAMS TRI study on detecting Parkinson's disease in voice recordings using ML. This new application uses ML in a way not thought possible. In another study, a small company in Canada has published data about diagnosing high blood pressure and type 2 diabetes through voice recordings. This approach appears to be at the cusp of reimagining ways to deliver health care.

In closing, Dr. Kurilla called attention to the 2024 Fall CSTA Program Annual Meeting, scheduled for November 13–15 in Rockville, MD.

Discussion

Annie M. Kennedy, B.S., asked when the various technologies, especially AI/ML products, would be available to help shorten the diagnostic odyssey, optimize outcomes, and deliver treatments faster for patients with rare diseases. She also asked about policies in place for protections against using these technologies to identify patients with rare diseases and discontinuing their insurance coverage before patients are aware of such diagnoses, as well as about funding to support such policies. Dr. Kurilla recalled similar concerns with the arrival of genome sequencing. The naïve thought was that a small fraction of the population would have genetic disorders and would be excluded from health insurance because of their preexisting condition. Congress resolved that problem by requiring insurance companies to cover preexisting conditions. Lessons from genome sequencing suggest that the majority of the general population does not have totally healthy genomes, but rather has multiple genetic mutations that subtly effect health and influence risk factors. Reimagining how health care is delivered because of the application of AI/ML points to reimagining how health care systems themselves are envisioned. The academic community needs to provide rigorous evidence, design appropriate clinical trials, and understand all the regulatory requirements to support the migration to a more equitable health care system that would be beneficial to everyone. He commented, however, that the policy decisions are beyond the academic or medical communities.

Joni L. Rutter, Ph.D., noted that discussions at the Food and Drug Administration and CMS about new treatments that are being developed for rare diseases and clinical trials do not necessarily reflect the age groups needing the therapies and may not be on the right path for decisions to be made about accessing those therapies that have had limited testing. Part of this discordance in trials is understanding ways to develop research questions while conducting research to consider forward-looking policies that might also be needed. From Dr. Rutter's perspective, these inquiries regarding gene therapy, gene editing, and other modalities are now being asked at the therapeutic level.

VIII. PROGRAM UPDATE PRESENTATION AND DISCUSSION: Office of Drug Development Partnership Programs (ODDPP): Christine M. Colvis, Ph.D., Director, ODDPP, NCATS; Karlie R. Sharma, Ph.D., Program Director, ODDPP, NCATS

Christine M. Colvis, Ph.D., provided an update on ODDPP activities and acknowledged the ODDPP staff and NIH Office of Data Science Strategy DATA Scholars supporting this office. She noted that ODDPP's work encompasses four general areas of support: (1) target landscape expansion that focuses on early drug discovery; (2) drug development partnerships across the pipeline that encourage and incentivize teams; (3) technology development, including such programs as the Awards Supporting Cutting-Edge Technology for Translational Science; and (4) data science and AI efforts that include the Biomedical Data Translator Program and LitCoin. She focused her update on expanding the target landscape.

Dr. Colvis explained that ODDPP uses a two-pronged approach to expanding the target landscape. The first approach is exploring understudied druggable proteins, which are proteins with a binding site where a small molecule, chemical, or drug could bind and modulate the activity of that protein. The second approach is drugging the undruggable targets, such as unstructured or misfolded proteins that do not have binding sites that can be modulated.

Illuminating the Druggable Genome (IDG)

Dr. Colvis noted that IDG, a 10-year Common Fund program, is coming to the close of its funding. The goal was to improve understanding of the properties and functions of understudied proteins within druggable protein families. Understudied proteins refer to those with few or no publications and/or lack of R01 funding. The NCATS Small Grant Program (R03) was established in 2019 to examine understudied proteins associated with rare diseases.

Karlie R. Sharma, Ph.D., who has been the IDG coordinator since 2019, provided a pre-closeout report of the IDG and began with a brief background. The druggable genome is the subset of the human genome that expresses proteins that can potentially bind drug-like compounds. Although the druggable genome contains an estimated 3,000 to 4,500 proteins, only 100 to 200 of those proteins are included in the clinical pharmacopeia, resulting in significant biology left unexplored. Three protein families were studied in the IDG: ion channels, G-protein-coupled receptors, and kinases. Dr. Sharma emphasized that IDG was selected as a Common Fund program because it investigated a topic area with broad applicability. She acknowledged the IDG leadership, including the IDG Working Group composed of representatives from across NIH.

- **IDG Program Timeline and Budget.** The pilot phase of the program extended from FY14 to FY17 and was allotted a budget of $25.5 million. The goals were to adapt scalable technology platforms for the IDG protein families and to develop a knowledge management platform. The implementation phase began in FY18, with a budget of $71 million. The goals of this phase were to identify phenotypes of understudied protein families, provide reagents and tools to the scientific community, and create an enriched, mineable knowledge base. Dr. Sharma noted that NCATS is leading the way in identifying dark and lost proteins and putting them in the context of human disease.

- **Implementation Phase Consortium.** The IDG program depended on a consortium structure for success. The consortium consists of three centers: Data and Resource Generating Center (one for each protein family), a Knowledge Management Center (KMC), and a Resource Dissemination and Outreach Center (RDOC). The program sponsored awards to deploy cutting-edge informatics IDG tools; R03 pilot projects to elucidate function in human disease, and Small

Business Innovation Research (SBIR)/Small Business Technology Transfer awards to initiate early research leading to commercialization.

Dr. Sharma noted that the publications attributed solely to researchers who were not IDG program awardees steadily increased over the years following the implementation phase of the program. The program awardees had a consistent increase in publications over the course of the program, and their work remains heavily cited.

- **Pharos Interface.** One major output from the IDG is the Pharos interface for the KMC. Pharos extracts data from the IDG, other Common Fund programs, and publicly available resources, such as Chemogenomic database (ChEMBL) and PubMed. Pharos accesses roughly 80 data sources and allows users to search the entire human genome for any target of interest, with the capacity for searches associated with diseases and ligands. Unique to Pharos is the ability to assign a target development level to each protein in the human genome. Four levels are featured: target dark (Tdark) (no information is known) Tbio (no known drug or small-molecule activities, but some publications and data exist), Tchem (at least one bioactive drug-like compound) and Tclin (at least one approved drug). Other features include a visualization tool and information on approved drugs and active ligands, protein–protein interactions, pathways, and structures (traditional and predictive). Pharos averages 3,000 users monthly and has affected target development levels by moving dark proteins closer to clinical status. IDG, the Structural Genomics Consortium, Open Targets, and Target 2035 are collectively working to address dark proteins.
- **R03 Pilot Projects.** The first R03 was awarded in 2019, and 98 have been awarded over the course of the program. The award size, $100,000 annually, supported direct costs. The awardees studied more than 120 Tdark proteins and have published more than 100 articles. The R03s funded 29 early stage and new investigators and has enabled 27 follow-on awards, both within NIH and externally. Dr. Sharma highlighted a project that advanced a dark protein to a clinical target. J. Stephen Lodmell, Ph.D., M.S., at the University of Montana and his laboratory investigated the Rift Valley Fever virus and identified a role for adapter protein, Right Open reading frame protein Kinase 3 (RIOK3), in antiviral immunity and the inflammatory reaction. Dr. Lodmell partnered with DermaXon, LLC, on an SBIR grant to develop RIOK3 as a novel therapeutic target for cutaneous lupus and has generated proteolysis targeting chimeras (PROTACs) that bind to RIOK3 with nanomolar affinity.

Dr. Sharma highlighted new partnerships and uses of IDG program resources. In 2022, IDG partnered with the Common Fund's Knockout Mouse Phenotyping Program to develop 27 understudied ion channel knockout mouse models. This work is in progress. Fondazione Telethon, an Italian nonprofit, and Fondazione Cariplo, a private philanthropic organization, are in alliance to investigate treatments for patients with rare diseases. Fondazione Cariplo used Pharos to identify the connection between Tdark proteins and rare diseases. To date, 59 projects have been funded, amounting to a €13.4 million investment by Fondazione Cariplo.

IDG Program Outputs: Impacts on the Future

Dr. Sharma highlighted the impact and future direction for IDG. Several options are being explored to maintain Pharos and ensure the interface is sustainable. The R03 Pilot award successes are still being reviewed, and reports are pending. The Common Fund and NIH ICs are incorporating a pilot program format into other initiatives. Several resources are publicly available. Interest in understudied protein families has increased. IDG demonstrated the value of these targets to human disease. She called

attention to additional publications from IDG grantees added to the Druggable Genome Special Series in *Drug Discovery Today,* which has featured IDG publications.

LitCoin Program

Dr. Colvis explained that the main goal of LitCoin is to build machine-readable, AI-ready knowledge from the literature. This process can involve either prospectively using newly submitted information, which would be the LitCoin publication format, or retrospectively using the existing literature for the Lit2Graph. The LitCoin publication format is being developed and will be activated in the future. The Lit2Graph can be generated today and involves uploading a human-readable abstract. The key to extracting knowledge is to computationally distinguish the novel information from the background. The Semantic MEDLINE (SemMed) database is the primary benchmark standard. The secondary benchmark is algorithm comparison with human calculation.

Discussion

Paula K. Shireman, M.D., M.B.A., commented on the rich data sets LitCoin will generate for AI/Machine Learning algorithms. She asked about a release date for LitCoin. Dr. Colvis explained that Litcoin has another year of funding from the Helping to End Addiction Long-term® (HEAL) Initiative, or NIH HEAL Initiative®. The goal is to work on extremely focused literature that will be relevant for pain. Next researchers will begin to socialize the program into the community to test the system. Tyler F. Beck, Ph.D., added that they are anticipating that the first HEAL-focused graph, the pain and addiction focused graph,, will be released in the early spring. The aim then would be to have the HEAL investigators fine-tune the graphs and retrain the model to improve its accuracy based on feedback. The next step will involve expanding to other fields.

Krishna (Balki) Balakrishnan, Ph.D., M.B.A., asked whether the percentage of information coverage necessary to make a useful LitCoin graph is a theoretical threshold. Dr. Beck explained that graphs generated using the LitCoin algorithm with other NCATS programs, such as the Biomedical Data Translator, would work with any percentage of coverage because the contextual knowledge of the peer-reviewed literature being used is vast.

Dr. Beck commented that the LitCoin Knowledge Graph contract was awarded to Research Triangle Institute (RTI) International and is funded by the NIH HEAL Initiative. RTI is working with CoVar, LLC, to generate these graphs along with a simple interface to display the outcome of the abstract and the author. Dr. Colvis added that Hackathons are being planned to bring together postdoctoral fellows and graduate students to evaluate the results of the graphs compared with the abstract.

Kelly Marie McVearry, Ph.D., Ed.M., asked about a sustainability plan for LitCoin beyond the HEAL Initiative funding. Dr. Colvis is optimistic that a funding source will be identified to continue the program, which has gained interest and enthusiasm in the scientific community.

IX. CLEARANCE OF CONCEPTS: Presentation and Discussion

The Council received presentations on two new initiatives and one renewal initiative that NCATS is considering funding. After each presentation, the members discussed the proposal and voted on whether to approve NCATS' moving forward with the concept. Discussants for the concept were assigned prior to the meeting.

Introduction of Office of Drug Development Partnership Programs Concept: Christine M. Colvis, Ph.D., Director, Office of Drug Development Partnership Programs (ODDPP), NCATS

Dr. Colvis noted that the ODDPP update presented earlier in today's meeting focused on the first approach to expanding the target landscape. This concept is addressing the second prong of drugging the undruggable targets.

Expanding the Target Landscape by Drugging the Undruggable Concept: Karlie R. Sharma, Ph.D., Program Director, ODDPP, NCATS

Karlie R. Sharma, Ph.D., presented a new concept on expanding the target landscape by drugging the undruggable. Traditional drug discovery relies on small biological molecules' binding to proteins for interactions. Many conditions are considered intractable due to pathologies that lack treatment development options or mechanisms that cannot be treated using traditional drug therapy. An intractable disease is not easily treated, relieved, or cured, or it cannot be treated, relieved, or cured through available therapies. Approximately 10 percent of the human genome is druggable, and 5 percent is druggable and disease relevant. Sixty percent of disease-related proteins are understood to be undruggable, and drugs have been launched into the clinic for only 13 percent.

Proteins that are classified as undruggable disease drivers include intrinsically disordered or misfolded proteins and are potential targets for developing treatments. Many diseases can be attributed to Ribonucleic acid (RNA) dysregulations, providing a research opportunity to address upstream targets. Molecular entities, such as lipids and metabolites, also have been linked to diseases. Numerous diseases — including neurological diseases, rare diseases (e.g., myotonic dystrophies), and cancer — are caused by these undruggable targets. Leading researchers in this field of investigating undruggable targets have had success at drugging these targets, leading to promising treatments. NCATS collaborated with three other institutes and centers to host a workshop on innovative molecular treatment modalities for intractable disease targets. The outcome of the workshop, "New approaches for challenging therapeutic targets," has been published in *Drug Discovery Today.* The main messages are that this research field is prime for new classes of molecular entities and alternative modalities and proof-of-concept strategies for drugging difficult targets are needed.

NCATS is proposing this concept to explore novel target classes to treat human disease. The overarching objective is to support preclinical development of treatments for diseases that have traditionally undruggable targets. This new initiative will fill gaps and relieve pressure points preventing or slowing the development of treatments for intractable human diseases and those diseases associated with undruggable targets. Each project will serve as a use case that demonstrates modulation of a traditionally undruggable target. Key aspects of this initiative are to expand the therapeutic pool of target classes and diseases, encourage significant process improvement for identifying novel targets for disease, and address patient populations that traditionally have unmet needs.

NCATS anticipates that this initiative would address those target classes with unmet needs and provide proof-of-concept studies, spurring innovation in new treatment modalities. The success of the concept would be the future development of treatment options for patients who endure these intractable diseases.

Discussion

Kelly Marie McVearry, Ph.D., Ed.M., asked about plans to work with the pharmaceutical industry. Dr. Sharma explained that the focus is on a starting point to interrogate undruggable targets, design platforms for the studies, and identify ways to drug those targets. The Small Business Innovation

Research program may be one option for supporting this research. Dr. McVearry suggested incorporating diseases of aging, neurodevelopment, and multiple rare diseases in the undruggable categories.

Robin J. Mermelstein, Ph.D., suggested applying an equity lens as described earlier in this meeting in considering the intractable disease groups.

Paula K. Shireman, M.D., M.B.A., emphasized critically reviewing and selecting platforms (e.g., lipid, metabolomics, proteomics) for investigating these undruggable targets and rigorously testing these platforms, which may require collaborations to advance the research. Dr. Shireman commented that AI results cannot always be trusted and referred to the LitCoin program discussed earlier.

Dr. Sharma pointed out that many existing platforms are specifically focused on developing small molecules or biologics, which limits opportunities for other target classes that may not fall within this category.

Matthew D. Hall, Ph.D., commended the ODDPP update and concept presented and asked about incorporating any tools or methods (e.g., proteolysis targeting chimeras (PROTAC) of the IDG program. Dr. Sharma noted that the PROTAC technology is cutting-edge but has been in use for some time. Newer technologies, such as deubiquitinase-targeting chimera (commonly called DUBTAC) that stabilize rather than degrade the protein, are being explored.

Dr. McVearry underscored that NCATS' vision (more treatments to all people more quickly) is an accelerator likely to have the rate of discovery outpace the existing funding mechanisms. Dr. Wayman appreciated the comments, which highlighted ways NCATS can synergize within the center.

Members unanimously approved the concept of expanding the target landscape by drugging the undruggable concept.

Introduction of the Office of Special Initiatives (OSI) Concept: Danilo A. Tagle, Ph.D., M.S., Director, OSI, NCATS

Danilo A. Tagle, Ph.D., M.S., explained that the OSI mission is to address translational problems with innovative solutions through disruptive technologies and novel partnerships with patient advocacy groups and other government agencies. All the programs within OSI adhere to NCATS' operating principles of "the three D's": developing the technology, demonstrating its utility, and disseminating the technology for use by the community. OSI soon will sponsor a prize competition in its Quantum Biomedical Innovations and Technologies (or Qu-BIT) program. This new concept builds on two technologies: (1) extracellular RNA (ExRNA) communication and (2) tissue chips/microphysical systems (MPS) for drug screening.

Selective Precision Targeting Concept: Christine M. Happel, Ph.D., Program Officer, OSI, NCATS; Passley Hargrove-Grimes, Ph.D., Program Officer, OSI, NCATS

Christine M. Happel, Ph.D., presented a new concept for selective precision targeting, which leverages the ExRNA Communication Program and the NCATS Tissue Chips for Drug Screening program. Some interventions require the safe and effective delivery of molecules to specific cells and tissues. These interventions include gene editing, monoclonal antibodies, or gene expression modulation.

NCATS proposes selective precision targeting to determine a mechanism for precise and on-target therapeutic drug delivery to specific hard-to-reach locations within the human body using MPS. Targeted drug-delivery systems, including nanoparticles or focused ultrasound, are methods for

delivering medications to a specific area of the body (organ, tissue, or cell) to increase the concentration of the drug in that area. Hard-to-reach locations in the body include the blood–brain barrier, central nervous system, placenta, retina, or a tumor.

Passley Hargrove-Grimes, Ph.D., explained that MPS or tissue chips are small, bioengineered devices capable of growing functional human cells and tissues for testing; specific targeting; and safety, efficacy, and toxicity assessments. MPS contain multiple cell types and are more physiologically relevant and predictive of *in vivo* biology than traditional models. Once linked to an integrated platform, MPS enable tissue communication across diverse biological barriers.

The objective of this concept is to provide evidence of therapeutic targeting to specific hard-to-reach locations within the human body using predictive multiorgan MPS. The focus will be on elucidating the targeting mechanisms with multiorgan human MPS and testing a broad spectrum of therapeutic cargo, including drugs, RNA, or gene-editing tools. The program goals are fourfold: (1) optimize specific targeting and therapeutics to the target or organ cell of interest, (2) assess biodistribution and off-target effects in a multiorgan human MPS, (3) provide evidence of functional cargo activity, and (4) determine the optimal route of administration.

Metrics for success will include demonstration of the ability to precisely target a cell or a tissue type of interest using the MPS and research activities and results that enable treatments for hard-to-treat diseases. NCATS anticipates the long-term outcome of clinical use of a targeted therapeutic for a highly specific disease context.

Discussion

In response to a question from Paul A. Harris, Ph.D., about preliminary data illustrating how cells respond in multichip systems, Dr. Hargrove-Grimes confirmed that these studies had been conducted. She noted that when integrated into platforms, the multi-tissue chips provide better understanding than single-tissue chips of where the drug will be distributed systemically, which also has been demonstrated in the published literature. Dr. Tagle added that several models of multiple organs-on-a-chip exist and are commercially available.

Kelly Marie McVearry, Ph.D, Ed. M., asked about the differences in responses between experimental cells and diseased cells, meaning cells from a patient diagnosed with a rare disease. She also speculated on the response if the starting point was from a tissue-on-a-chip that was a pluripotent stem cell from an individual with a rare disease. Dr. Hargrove-Grimes pointed out that in the Clinical Trials on a Chip program, 9 of 10 research teams have switched from using primary cells to using pluripotent stem cells and have generated improved patient-specific tissue-chip models. Regarding the differences in cells, OSI is encouraging researchers to use only patient-derived primary cells rather than cell lines in these studies, especially because most cell lines lack genetic diversity. Dr. Tagle noted that one advantage of tissue chips is the ability to use patient-derived samples to generate pluripotent stem cells. He added that for more than 5 years, OSI has used a control cell line to perform somatic gene editing to introduce a mutation, thus controlling the allelic background and homing in on the mechanism of pathogenesis.

Dr. McVearry noted that such somatic editing experiments are doing more than replacing animal models in preclinical studies and are eliminating such parallel comparisons in trials. Dr. Rutter added that NCATS hopes the Tissue Chips for Drug Screening program will lead to having tissue chips replace animal models in trials, but further studies are needed. She questioned whether development of standards could be incorporated into this concept to ensure that appropriate comparisons of models are being made. Dr. Tagle provided a few examples regarding patient diversity in tissue chips. More than 250 pluripotent stem cell lines of Hispanic origin are being used to study metabolic-associated steatotic liver

disease (MASLD); the Hispanic population is vulnerable to increased diagnosis of MASLD. Also, biospecimens from more than 50 male donors are being used to study prostate cancer.

Paula K. Shireman, M.D., M.B.A., emphasized interrogating both negative and positive responses to and off-target effects of treatment in the tissue chip trials to better understand these differences because cells communicate with their environment, which would be reflected in their responses.

Sharie J. Haugabook, Ph.D., asked about the justification for mixing the multiple cell types in the models being developed for drug screening. Dr. Happel confirmed this justification and noted that the multi-organ (i.e., multiple cell types) chips are recapitulating the normal physiology to ensure accuracy in model development. Dr. Hargrove-Grimes commented that NCATS has the tools and has evaluated the responses of multi-organ tissue chips designed using biospecimens for different patient populations and can delineate those responses.

Members unanimously approved the selective precision targeting concept.

Introduction of Division of Rare Diseases Research Innovation (DRDRI) Concept: Phillip John (P.J.) Brooks, Ph.D., Deputy Director, DRDRI, NCATS

P.J. Brooks, Ph.D., explained that DRDRI directs programs and initiatives across three areas: (1) patient support and information; (2) funding research and development programs; and (3) convening and partnering activities. This new concept crosscuts the first and last areas and will strengthen investigating many rare diseases at a time.

Rare Diseases Are Not Rare! (RDANR!) Challenge 3.0 Concept: Ainslie Tisdale, M.P.H., Health Specialist, DRDRI, NCATS

Ainslie Tisdale, M.P.H., presented a renewal concept on the RDANR! Challenge 3.0. The collective burden of rare diseases has garnered a groundswell of attention. Four studies published in 2021 conveyed the overall message that rare diseases are costly, both in economic and human terms. Patients with rare diseases are underrecognized and underprioritized in health care systems and databases. These studies illustrate that rare diseases are a public health problem that requires increased attention, awareness, and education.

NCATS hosted RDANR! Challenges in 2018 and 2020 that focused on raising awareness and fostering collaboration across rare disease communities, including patients, caregivers, and advocates. The challenges have resulted in several creative communication pieces, such as posters, videos, and infographics that have been widely shared. The winners and honorable mentions are featured at Rare Disease Day at NIH, and the first-place winner is invited to speak at the event. The RDANR! Challenge 1.0 winner was a parent of a child with a rare disease who created posters raising awareness for rare diseases and the people they affect, emphasizing the message that rare diseases are not rare. Further details can be accessed from NCATS Challenge and Prize Competition Winners webpage. The first-place winner of Challenge 2.0 was a rare disease patient and advocate who submitted a video of himself reciting a poem he wrote to raise awareness of rare diseases; he also received a Zebbie award for the challenge.

Historically, the approach to messaging about rare diseases has focused on developing treatments for one disease at a time and on increasing funds for this research. This message led to the public perception that rare diseases are individual problems rather than as a collective problem that requires a larger solution. Data show that more than 10,000 rare diseases exist and only 5 percent have treatments. The one-disease-at-a-time approach does not lend itself to NCATS' reaching its audacious

goals of more treatments for all people more quickly. Changing the messaging that rare diseases should be approached collectively and in a many-diseases-at-a-time approach will be critical. Public messaging about rare diseases and rare disease research has existed for more than 40 years — starting with the Orphan Drug Act of 1983 — but that message has not been unified, which has widely affected the amount of funding received for rare disease research.

NCATS proposes this concept to raise awareness for rare diseases and all the people they affect collectively. The intent is to highlight the need for crosscutting research and development of new treatments and to increase meaningful engagement with the rare diseases community. The objectives are to seek innovative ways to communicate with others and educate the public through patient-generated art, shift public perception of rare diseases being rare, increase messaging about addressing many rare diseases at a time, and provide an opportunity for patients or patient advocacy groups to be funded by NCATS.

The RDANR! Challenge 3.0 is aligned with NCATS Strategic Plan goals and seeks to impact the research community by fostering innovation and collaboration and increasing awareness about rare diseases. Submissions can include various media types, posters, infographics, or animated graphics. This concept will leverage ongoing activities at NCATS, including the many-diseases-at-a-time programs, and will offer a means to collect and broadcast how this theme is being portrayed and accelerated in the community. The RDANR! Challenge 3.0 also will leverage NCATS Office of Policy, Communications and Education Communications Branch campaigns to educate the community about, and raise awareness of, rare diseases.

NCATS expects this concept to foster innovation and collaboration; increase awareness of and highlight potential funding opportunities; build the community knowledgebase; encourage cross-disciplinary research with broad perspectives and novel approaches; and raise awareness about NCATS' central role in the rare diseases community. The success of RDANR! Challenge 3.0 will be observed in receiving more than 30 submissions, increasing visits to the NCATS rare disease-related web pages, creating communication mechanisms, releasing social media campaigns, and increasing collaboration and networking.

Discussion

Annie M. Kennedy, B.S., highlighted the Everylife Foundation study alluded to earlier, which examined direct medical cost data and indirect and nonmedical data that had been collected through a survey developed by more than 300 patient advocacy groups. These groups, which registered their membership and disseminated the survey throughout their communities on the Foundation's behalf, can help announce the RDANR! Challenge 3.0. The Foundation facilitated the data analysis and dissemination of findings from that survey to leaders in academia, industry, and government, including NIH. Ms. Kennedy underscored that the rare diseases community has become adept at communicating about the impact of the collective economic burden. Messaging about this new challenge can be paired with the studies that NCATS has led and published on the topic and other opinion pieces that demonstrate the collective nature of rare diseases. She noted that Everylife coordinates the Congressional Rare Disease Caucus and leads an annual rare disease artist campaign and reception on Capitol Hill. She also suggested partnering with groups that are interested in sponsoring public health campaigns about rare diseases, such as Global Genes.

Kelly Marie McVearry, Ph.D., Ed.M., asked about considering a digital component that allows media submissions to be minted rather than submitted; the submission could become a non-fungible token, which would preserve the artist's property rights. Dr. Tisdale noted that the two previous challenges

contained specific language that NCATS/NIH would own the submitted item. She will follow up with DRDRI and report back to the Council at a future date.

With the previous two challenges and with this proposal of a third challenge, Robin J. Mermelstein, Ph.D., suggested evaluating the program and examining its reach to the community, the diversity of participation, and the rare diseases highlighted. Dr. Tisdale agreed and will consider this suggestion when planning and promoting the RDANR! Challenge 3.0. She noted that DRDRI will review the Rare Diseases Day reach, which has included more than 10 countries, and that Dr. Brooks can revisit conversations with the International Rare Diseases Research Consortium. She pointed out that although international groups would be eligible to submit their ideas, the financial prize would be awarded only to U.S.-based groups.

Members unanimously approved the RDANR! challenge concept.

X. PUBLIC COMMENTS

Public comments were accepted until October 10, 2024 (15 days after the meeting) and will be appended to the minutes.

XI. ADJOURNMENT OF THE OPEN MEETING

Joni L. Rutter, Ph.D., thanked the participants for their input. The next meeting is scheduled for January 30–31, 2025 and is planned as a virtual session. Dr. Rutter adjourned the meeting on September 19, 2024, at 5:05 p.m. ET.

XII. CERTIFICATIONS

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

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Joni L. Rutter. Ph.D. Date
Chair, NCATS Advisory Council
Director, National Center for Advancing Translational Sciences (NCATS), NIH

_____ _____

Anna L. Ramsey-Ewing, Ph.D. Date
Executive Secretary, NCATS Advisory Council
Director, Division of Extramural Activities, NCATS, NIH