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Good morning, everyone. Welcome to our first NIH Council of Councils meeting in 2025. I'm going to bang the gavel. This meeting is now in session. I am Nicole Kleinstreyer. I'm the acting Deep Kipsy director, and it is a pleasure to be with you all today and to meet you all virtually. And I look forward to meeting you in person in our next meeting. I'll introduce myself and tell you a little more about me later this morning. I am joined here by Dr. Francesca Grider, who serves in the role of the Executive Secretary of the Council of Councils and Director of the Office of Research Infrastructure Programs. Additionally, I would like to recognize my Deepa Kipsi colleagues in the room: Robin Kawazoe, Deputy Director of Deepa Kipsi. Grace McCarthy, Health Science Policy Analyst.

Also joining us virtually are Taylor Gilliland, Senior Scientific Advisor to the DPCPSI Director, and Bettina Orozoli, Program Analyst and Council of Councils Coordinator. I would like to thank the Council Meeting Planning Team members for all of their work in support of all of the Council activities. I would also like to recognize the Logistics Contractor for the Council of Councils, the Scientific Consulting Group, or SCG. And before we really get going, let me just turn it over to Francisca to remind you of a few procedures before taking roll call to ensure today's meeting runs smoothly. Great. Thank you, Nicole. And good morning, everybody. It is good to see you, at least virtually, all today. And I'm also looking forward to the May meeting where we will all be in person.

We will remind you of some rules which will help to ensure that are able to contribute: we ask you to remain muted when you are not actively speaking to the group; if you would like to make a comment or ask a question, please use the raised hand feature. You all noticed we are today on Teams, that's a little bit new for all of us, not just Teams in general but Teams and Council. So, please use your raised hand feature and/ or enter a comment and/ or question directly in the chat box. One of us will call on you, and we will use the raised hand feature first and the chat box second. If you have technical difficulties, please contact Danielle or Allison-their names and contact information is displayed on the monitor on the slide right now.

If you have challenges or problems with ECB, the Electoral Council book, please contact Bettina via chat box or the number displayed as well on the screen. So, we will next do roll call at this time. We have done this many times before, so you're well aware of how we are doing this. Please tell us your name, your institutional affiliation, and indicate if you have served on a council before and which council. I will call your names in alphabetical order. Once I call your name, please unmute yourself and then introduce yourself. So here we go. Dr. Kristen Ardley, you are up first, Dr. Ardley. Hi, I'm Kristen Ardley. I'm at the Broad Institute, and I have not served on any previous councils. Thank you, Kristen. Dr. Linda Chang. Linda? Yes, hi.

I'm Linda Chang from University of Maryland in Baltimore. I previously served on the BSC at NIDA and also at the NIDA Council. Thank you. Thank you, Linda. Dr. Monica Gandhi. Dr. Gandhi? Yes, I'm Dr. Monica Gandhi. I'm a professor of medicine at UCSF, and I previously served at NIAID Advisory Council. I'm an infectious disease researcher. Thank you, Monica. Dr. Rafael Irizarry. Hi, my name is Rafael Irizarry. I'm the chair of the Department of Data Science at

Dana-Farber Cancer Institute, and I'm also a professor of applied statistics at the Harvard School of Public Health. I served in the council for the NHGRI. Thank you, Rafael. Dr. Kevin Johnson. Good morning. I'm Kevin Johnson. I'm a university professor here at the University of Pennsylvania. I'm a pediatrician, researcher, and biomedical informatics person.

And I previously served on the NCRR council. And on the Board of Scientific Counselors for the NLM. Thank you, Kevin. Dr. Karen Johnston. Hi, I'm Karen Johnston. I'm at the University of Virginia and I previously served on the NINDS Council. Thank you. Thank you, Karen. Barbara Kelly is not with us today. She has other obligations. Dr. Jean King. Yes, I am. Oh, so sorry. So sorry. My information is incorrect. No, it's good. I'm traveling, so I'm in and out. Thank you. I'm Barbara Kelly. I'm Executive Director of the Hearing Loss Association of America, and I previously served on the NIDCD Council. Great. Thank you, Barbara, and thank you for making the effort. Dr. Jean King. Dr. King? Dr. King, please unmute yourself and go ahead. Can you help, Christine? Dr. King? Yes. Can you hear me? I have been trying. Sorry. I have no idea why it's not working.

We could hear you, Dr. King. You're on mute again.

All right, Gene, let's go to the next person, and I'll come back to you at the very end for introductions. Let's go to Dr. Richard Krugman next. Dick? I'm Dick Krugman, a distinguished professor of pediatrics at the University of Colorado School of Medicine and work at the Kemp Center for Prevention of Child Abuse and Neglect. Thank you. Sorry, was on the NICHD Council for four years before joining this one. Great. Thank you, Dick. Sorry, I was over-eager. Next is Dr. Kent Lloyd. Good morning, everyone. My name is Kent Lloyd. I'm a professor in the Department of Surgery, Associate Director of our Comprehensive Cancer Center at University of California, Davis, and I served on this Council of Councils previously. Thank you. Thank you, Kent. Dr. Jennifer Manley.

Jennifer?

Dr. Manley, please unmute yourself and go ahead.

Dr. Manley, I see you are unmuted. Please let us know if you are having issues, and we will do our best to assist. All right, Jennifer, let's move on, and I'll get back to both you and Jean later on. Next is Dr. Rhonda Robinson-Beal. Rhonda Robinson-Good morning. Rhonda Robinson-Beal. I'm a psychiatrist by background, and I am an SVP and Chief Medical Officer for Mental Health Services for UnitedHealth Group. I served prior to this council with the National Advisory Mental Health Council for six years. Thank you, Rhonda. Dr. Susan Sanchez. Good morning, everybody. I'm Susan Sanchez. I'm a professor of infectious diseases at the College of Virtual Medicine at the University of Georgia, and I have not served in other council before this one. Thank you. Thank you, Susan. Dr. Anne-Maria Segariz.

Yes, good morning. I am the Dean of the School of Public Health and Health Sciences at UMass Amherst. I'm a professor of nutrition and in the Department of Epidemiology and Biostatistics. I

have previously served on NHLBI's Advisory Council. Thank you, Ana Maria. I understand Lauren Silves is not on, correct? Yes. And then the last one on the list, sorry, was Dr. Russ Van Gelder. Hi, Russ Van Gelder, Professor and Chair of Ophthalmology at University of Washington in Seattle. I've previously served on the Council of the National Eye Institute. Thank you, Russ. Let's try again, Dr. Jean King. Jean, can you hear us and can you introduce? I can. Hi. Oh, excellent. Yes. For some reason, my computer was not allowing me to unmute myself. My name is Jean King. I'm the Peterson Family Dean of Arts and Sciences at Worcester Polytechnic Institute in Worcester, Mass. I'm also an affiliate faculty in psychiatry, radiology, and neurology at UMass Medical School, also in Worcester, Mass. And I served previously on NCCIH Council. Wonderful. Thank you, Jean. I'm glad it worked out. So let's give Dr. Jennifer Manley another try. Jennifer?

Alright, well maybe we'll try another time uh Jennifer and uh we are glad you are here and we hope you can hear us and then hopefully you can contribute in some way with that let me uh move on to a few more announcements that I have to make to get us going um meeting materials were sent to you for this meeting on April 16th, you received those materials via email. As members of this council, you are special government employees, and therefore subject to the rules of conduct that apply to all federal employees. These rules and regulations are explained in a report which is entitled Standards of Ethical Conduct for Employees of the Executive Branch, and you receive that report when you are first appointed to this council.

At every meeting, in addition to reminding you about the importance of following the ethics rules, we always like to review the steps that we take and ask you to take to ensure that any conflict of interest between your public responsibilities and your private interests are identified and addressed. Three times a year you provide us with information about your personal, professional, and financial interests. We use this information as the basis for assessing whether you have any real potential or apparent conflict of interest that could compromise your ability to be objective in giving advice during council meetings. If such conflicts are identified, we either issue a waiver or recuse you from a portion of the meeting. We also rely

to a great degree on you to be attentive during our meeting to the possibility that if an issue arises that could affect or appear to affect your interests in a specific way, if that happens we ask you to recuse yourself from the discussion and because this is a virtual meeting, you will be placed in a waiting room after you tell us in the chat that there is a conflict. If you have any questions about the rules of conduct or conflicts of interest, your committee or our committee management specialist, her name is Faye Smack, and you have interacted with her many times before, or I will be glad to address your concerns. For today's meeting, time is allocated in the agenda for discussions by the council, with the council, but unfortunately there is limited time for any comments from others, from other attendees.

The public is welcome to submit comments in writing after the meeting. Instructions for doing so are in the Federal Register Notice that was published for this meeting on March 25. Approved minutes for this meeting will be posted on the DPCC website. And with regard to future meeting dates, there are three ways how you can get those dates. They are always listed on your

agenda. They are always listed on the DPKIPC website. And of course, you can always email me and I will tell you as a reminder. Let me remind you again of the microphones, although Nicole told you, I told you, the meeting is being recorded and will be transcribed. Please unmute yourself when you speak and identify yourself. Also, please mute yourself.

after you have finished so others can turn their microphones on please note that the host of the meeting can control your microphone as well in case you have forgotten to turn yourself off and a reminder to turn on your videos and cameras if you are speaking if you need any any assistance the chat function is a good way to get assistance don't maybe send requests to everybody. You always can address very specific people. So finally, a closed session will be held from 12 . 15 to 1 o'clock today. In attendance, in accordance with NIH and federal policy, attendance is restricted to council members and relevant NIH staff. Following the closed session, we have a brief break for lunch, and we will resume the open session at 1:15.

Are there any questions at this time? All right. I'm not seeing any questions. Therefore, I'll turn the microphone back over to you, Dr. Kwanstroyer. Thank you, Francesca. So I would like to repeat that we are in the open session of today's meeting, which means open to the public, including members of the press. We are video casting this meeting, so all interested parties can listen. All right, let's kick things off. We have a very packed agenda, and certainly if you need to step away for a minute, we do understand. So after I provide some Deepa Kipsey updates, our agenda will include remarks from the NIH Director, Dr. Bhattacharya, four concept clearances, not in that order, actually. First, some concept clearances, then later in the day, remarks from our new NIH Director.

We will also have a presentation on a Council of Council workgroup on science of science. And we will close out the day with reflections from our departing council members. As you know, the directors of each of the DPCPSI program offices serve as non-voting liaisons to the council. They are listed here with their photos on this slide. And they are also on the call and available for inputs or comments if needed. I want to take a moment to note that Stefan Pasiokas left his position as the director of the Office of Dietary Supplements for an opportunity in academia. And Drew Bremer, the director of the Office of Nutrition Research, has kindly agreed to temporarily serve as the acting director of ODS.

Also, in alignment with the administration's executive order on defending women from gender ideology extremism and restoring biological truth to the federal government, NIH is terminating groups that do not align with that EO. This includes the Sexual and Gender Minority Research Office in Deepakipsi and the Council of Councils Sexual and Gender Minority Research Working Group. We will notify the working group members following this meeting of the dissolution of the working group. So now to turn to the Deepakipsi updates. So I want to start by announcing some exciting additions to Deepa Kipsey. First, myself, although that's less exciting than the next slide, which will talk about some formal additions of some programs. But just to say hello and introduce myself to all of you, I was privileged to be appointed the acting NIH Deputy Director for Program Coordination, Planning, and Strategic Initiatives on April 10th, so just under two weeks ago.

That of course means that I am also directing the Division for Program Coordination, Planning, and Strategic Initiatives. I have been a part of NIH for almost 10 years. I came from NIEHS, National Institute for Environmental Health Sciences, the Division of Translational Toxicology. I was the Director of the NTP Interagency Center for the Evaluation of Alternative Toxicological Methods, or NICEDM, also the Executive Director of the Congressionally Mandated Interagency Coordinating Committee for the Validation of Alternative Methods, which consists of 18 different federal agencies, including NIH and several institutes and centers within NIH. And there, I was really, really honored to be leading interagency and international efforts to develop and validate what are called NAMs. I'm sure all of you are familiar with that term, but there are new approach methodologies.

My personal background is actually in computational modeling, biomedical engineering, artificial intelligence, and systems modeling. And so I'm just really, really excited to be in this position and to learn more and more about Deepa Kipsi and the outstanding work that's being done across all of NIH, both within the Deep Echipsy offices and across all of the ICs. Okay. Moving to the next update, I am very pleased to announce the formal addition of the All of Us Research Program Office and the ECHO Program Office to Deepa Kipsey. We also integrated the management of the INCLUDE project into the Deepa Kipsey Director's Office. As you all are probably aware, Deepa Kipsey has informally welcomed them into the fold for the past year, so that process actually started at the end of 2023.

But we're very excited that these transformative programs are now officially in Deep Poughkeepsie. On September 24th, the Office of AIDS Research hosted the second Innovation in HIV Research Symposium. This was held during the NIH Research Festival. This was a hybrid event. It featured intramural investigators who received innovation program awards with 16 presentations covering assorted topics such as virology, vaccine discovery, data science, comorbidities, and co-infections. This symposium highlighted the program's impact in fostering innovative research with the potential to advance the HIV care continuum. Participants remarked that they appreciated the opportunity for networking and gaining insights into the intramural HIV research community. In December, OAR had a really incredibly busy and exciting month in honor of World AIDS Day. So, that was December 1st, and sort of kicked off a month of exciting activities.

OAR hosted a World's AIDS Day virtual panel. This was attended by over 500 participants, and that's notable because it's a 42% increase from 2023. Several OAR staff attended the first-ever White House display of the AIDS quilt. OAR leadership attended several national meetings and two congressional receptions honoring the retiring Representative Barbara Lee, who co-chaired and co-founded the HIV Congressional Caucus. On a sadder note, the team paid respects to Mr. Cornelius Baker, who was an OAR consultant and lifelong HIV advocate, and he was laid to rest at the National Cathedral on December 13th. Also in December, NIH announced awards to advance technology for HIV viral load detection. So funding and support services were awarded to three diagnostic technology developers as part of RADx, or the Rapid Acceleration of Diagnostics, these tech-advanced platforms for HIV viral load monitoring program.

So launched in the spring of 2024 by NIVIB in collaboration with OAR and NIAID, this program is aimed at advancing HIV viral load detection technologies for use at point of care. So the three awards that are listed here were SOFIED in California, which is point of care technology to quantitatively detect levels of HIV in under 90 minutes. Babies Incorporated from Durham, North Carolina, which is optimizing RT-PCR for HIV assay sensitivity, blood processing techniques, and viral load quantification capabilities. And Prompt Diagnostics in Baltimore, which is a magnetofluidic cartridge platform that facilitates automated infectious disease testing in the clinic and makes results available in less than 30 minutes. Then on December 17th and 18th, the ONR and FDA co-hosted a joint NIH-FDA nutrition regulatory science workshop.

The goal of this joint workshop was really to highlight how nutrition science can generate evidence and data to inform food-related policy and regulatory decision-making and to foster additional collaboration between NIH and FDA in supporting research that addresses priority nutrition research gaps. So there were many topics that were discussed at the workshop. These included ultra-processed foods, impact analysis, and implementation science related to regulatory actions, and emerging technological innovations related to nutrition regulatory science. Around the same time, December was quite a busy month; Thoreau, to the Tribal Health Research Office, held a two-and-a-half-day in-person federal Indian boarding school healing summit. So this summit brought together boarding school survivors, community practitioners, scientific leaders in intergenerational trauma research and intervention development, and leaders from multiple NIH ICOs and federal agencies. So the goal here was to share.

Identify gaps in knowledge, and align priorities for developing initiatives that embrace a whole-of-government and community-informed approach to addressing boarding school and intergenerational trauma healing. Then, most recently, ODS has released their strategic plan for 2025 through 2029. This strategic plan outlines three primary goals: advance research, expand capacity, and foster stewardship that will enable ODS to develop new research opportunities and promote resources to build understanding of how dietary supplements modulate resilience and health across the lifespan in heterogeneous populations. And then the Common Fund Venture Program, which you all heard discussed here, a new form of common fund support, is actually providing a framework to develop short-term projects with the potential for significant outsized impact, has recently launched its two initiatives.

So CISBio, the first of these initiatives, is an effort to integrate various data types that allow researchers to explore the role of a specific gene, molecule, cell, or pathway across tissues involved in different disease. and Oculomics to develop and apply novel non-invasive eye imaging technologies, machine learning algorithms, and other tools to identify highly sensitive and specific biomarkers for diseases that affect the entire body. So both initiatives made awards and held kickoff meetings. Then ODP is partnering with the CDC's Office on Smoking and Health to sponsor the Quit and Thrive Challenge, community-derived solutions to reduce menthol cigarette smoking. So the goal of this challenge was to showcase community-generated solutions that have reduced menthol cigarette smoking among groups

with disproportionately high rates of use. And, of course, that includes youth and minorities and people with lower incomes.

These solutions may be used to inform future federally funded research initiatives or demonstration projects. Up to nine prizes of $100,000 each will be awarded to winning organizations in July of 2025. So I really wish that I had more time to continue sharing all of the wonderful progress and updates we have as a division, but I will have to stop for now so that we can get to the rest of our agenda. And so the last thing that I'll do before we move into the concept clearances is that DPCC is actually leading development of the agency-wide NIH Strategic Plan for Disability Health Research. So this is a prospective effort that we're undergoing the planning and development process for right now.

So through the NIH Disability Health Research Coordinating Committee, we brought together subject matter experts from 24 ICs and 18 offices and programs to share research advances and collaborations. We also hosted six community roundtable discussions and a public town hall to gain insights from people with disabilities, researchers and clinicians, professional associations, and advocacy organizations. And then we also published an RFI to obtain public feedback on the draft framework for the strategic plan. And we received over 140 responses to that. So, the strategic plan will be released later this year. And after this meeting, we will be sending invitations to the Council of Councils Disability Health Research Working Group. Okay, so now we will be moving into the concept clearance portion of the agenda. So first up, we have a concept clearance from the Office of Research Infrastructure Programs, or ORIP. Dr. Ritesh Tandon, Program Director in the Division of Comparative Medicine in ORIP, will present a reissue of the concept entitled 'Limited Competition, Small Grant Program for ORIP Special Emphasis Research Career Award, or CERCA, K01 recipients.' R03 clinical trials not allowed. This presentation will be followed by comments from two assigned council member discussants, Dr. Susan Sanchez and Dr. Monica Gandhi. Ritesh, over to you. Dr. Good morning. Can you all hear me? Yes, thank you. Next slide, please.

We can't hear you now. Okay. Can you hear me now? Yes. okay can you see my camera no no no okay okay

So, Ritesh, it looks like your camera is blacked out, so I don't know if it's technical issues or if it's just a matter of switching it on. I get from my technical colleagues here a nodding that it's probably just a technical issue. So, why don't you just present and we just won't see you while you're presenting. That makes more sense to me. We can see you now. Okay, great. Now we can see you. Great. Thank you so much. So, good morning, everyone. I would like to briefly introduce for the concept clearance the reissue of the unique small grant program for OREP Veterinary Scientist Special Emphasis Research Career Award, CERCA K01 recipients utilizing the RO3 mechanism. The objective of this program is to facilitate CERCA K01 recipients' successful transition to independence by alleviating financial dependence on the mentor.

Demonstrating additional success and experience in peer-review competitions, and generating additional data and publications in support of future R01 or equivalent grant applications. The

funds available and the anticipated number of awards for this program are contingent upon NIH appropriations and how many meritorious applications are submitted in a given cycle. The award project period is for two years. And the council action that will be under discussion is a vote for continued support of the small grant program for ORIP veterinary scientists circa K01 recipients. Next slide, please. To give you some background on ORIP's RO3 program, ORIP supports circa K01 grants under the Mentored Research Scientist Development Award, Parent K01, for developing the career of veterinary scientists. The ORIP K1 program is unique at NIH because it specifically supports veterinary scientists and provides a mentored research experience to help early-stage veterinary scientists transition into independent investigators focusing on comparative medicine, biomedical research, and translational sciences.

Veterinary scientists bring unique knowledge of comparative biology that is important for the development and refinement of animal models of human diseases, as well as recommendations on alternatives to animal models. The transition from K grant to R grant is a critical career juncture. Recognizing the challenges of this phase, Several NIH institutes have successfully used limited competition R03 grant program to supplement the career development of their K grant recipients during the last two grant award years. The intent of these R03 programs is to increase the success rate of new investigators by applying for R01 or equivalent grants, which has been shown by other programs. Next slide, please. ORIP established its own RO3 program for SIRCA K01 grant recipients in fiscal year 2017, which has continued to evolve under ORIP's oversight.

This program enhances the ability of awardees to conduct research as they transition to becoming independent researchers and aligns with ORIP's mission to support research training opportunities for veterinary scientists. Since June 2017, three notices of funding opportunities or NOFOs have been issued and are listed here. I should mention that the NOFO was recently reissued at the end of March to align with administrative priorities. A single annual receipt deadline for previous NOFOs was a limitation that left many applicants with little or no chance of being eligible to submit an A1 application if their A0 application was not funded. Especially considering these are trainees eager to move on to their next career stage, the program changed the application receipt deadline to three times a year, starting with the 2023 NOFO. Next slide, please.

RO3 program aligns with the strategy 3. 1 of its strategic plan 20-21 to 20-25, which highlights promoting innovative approaches to training and developing the careers of veterinarians working in biomedical research, investing in training and mentorship innovations for the development of veterinary scientists as independent researchers and collaborative team scientists, and supporting the career development and training that prepares graduate veterinarians to pursue research that major gaps in biomedical and biobehavioral science and expands knowledge in emerging areas critical to human health. This R03 program provides access to research support that allows early-stage veterinary scientists to pursue unique research directions independent of the funding support of their mentors, facilitate their transition to independence, and increase their competitiveness for R01 or equivalent grants. Next slide, please.

The proposed R03 program initiative is intended to support research projects that can be carried out in a short period of time with limited resources and that may provide preliminary data to support a subsequent R01 or equivalent application. Projects that would be supported include pilot and feasibility studies, secondary analysis of existing data, small self-contained research projects, development of research methodology, and development of new research technology. Next slide, please. ORIF's RO3 program is limited to ORIF CERCA K01 awardees who are encouraged to submit an RO3 application after completion of the first two years or 24 months of their K01 award. However, they are ineligible if they have already successfully completed for an RO1 or equivalent award. At the time of submission, the CERCA K01 award must be active.

CERCA K01 awardees may receive funding for only one RO3 grant award, and RO3 applicants can request a budget up to $150,000 in direct costs for two years. Next slide, please. The program has achieved notable success since being established. With the first NOFO being released in fiscal year 2017, followed by receipt of the first round of applications eligible for submission in fiscal year 2018. 13 RO3 awards were made between 2019 and 2024 from among 42 applications submitted between fiscal year 2018 to 2024. This is a 31% award rate. In fiscal year 2025, seven of the 13 grantees have already applied for NIH RO1 grants, while three grantees have already been awarded RO1 grants. After receiving RO3 grants, seven grantees have advanced in following years to the rank of associate professor and one grantee to the rank of assistant professor.

The remaining grantees have maintained their positions with four grantees as assistant and one grantee as an associate professor. The 13 grantees collectively have 16 publications, 13 research, one review, and two clinical articles associated with their RO3 grants. 15 of these publications are senior author publications indicating the independent status of awardees. An analysis of the translational impact of these publications was done using iCite. a tool developed by the Office of Portfolio Analysis within the Office of the NIH Director. This tool generates a translational pyramid showing article density between human, animal, and molecular cellular research vertices with red and warmer colors reflecting a high article density while blue or cooler colors reflecting a low article density. As shown in the figure to your right, publications from these awards cluster between animal-oriented research and molecular cellular research, indicating that the awards primarily supported pre-translational research.

An upward movement to translational research is expected as the awardees progress further in their career. The program's outcomes demonstrate its effectiveness in supporting CERCA K1 awardees as they transition to independent and productive research careers. Next slide, please. For this concept clearance to address the ongoing need for transition support between KO1 and RO1 grants for veterinary scientists, ORIF requests that council vote for approval of the concept for reissue of a small grant program for ORIF veterinary scientists circa KO1 recipients utilizing the RRO3 mechanism. I'm happy to answer any questions during the discussion. Thank you so much. Thank you, Ritesh. Dr. Sanchez, would you please share any comments with the council? Thank you very much, Dr. Tandon and Dr. Grinster. I hope everybody can hear me. Is that correct? Yes, we can. Excellent.

So the National Institute of Health has always emphasized developing a robust physician-scientist workforce, including veterinary scientists. This recognition arises from veterinarians' crucial role in biomedical research and their unique contributions to comparative medicine. A large proportion of research awards use animals. Veterinarians are uniquely positioned to refine, reduce, and improve these models. And yet, they're a minuscule proportion of the NIH-funded scientists. NIH has implemented various training and career development programs to support veterinary scientists at different stages of their career. The Office of Research Infrastructure Programs supports the Special Emphasis Research Career Award circle through the K01 mechanism. These awards aim to enable these individuals to become competitive for academic research careers as independently funded biomedical scientists. These awards emphasize in-depth research experience for up to four years in various basic, preclinical, and translational science disciplines.

The research focus areas include laboratory animal models that identify, develop, and characterize both spontaneous and engineered animal models to enhance the understanding of human diseases. Unfortunately, transitioning from a training grant to an R01 award is difficult, as obtaining preliminary data is often limited to the laboratory with a trainee's training. To better prepare veterinary scientists to realize their true independence and receive funding for their research, and to maintain their laboratories, OREP has since 2017 offered a small grant program, the R01 Awards, for which only circuit recipients can apply after completing 24 months of their research under this award. The R01 duration is only two years, and its funding is limited to no more than $150,000 over this period.

The small grant awards aim to enhance the ability of veterinary scientists to conduct research and increase their chances of obtaining additional funding as they transition to becoming fully-fledged independent investigators. It helps improve their ability to obtain further funding in the form of another one or equivalent. It is essential to evaluate some metrics and to assess the success of the program as it extends. The overall funding rate of this award since the implementation has been 31%, which is pretty good. Of those RO3 recipients, three have obtained already RO1, which is already at 23 per success rate, and seven more have their RO1s currently under review. This is a significant achievement in the current climate and despite the pandemic. In addition, the number of publications seems reasonable, 16 overall, which is not bad considering the short term of these awards.

We are all aware of the time it takes to produce data and then write, while at the same time preparing and writing your next big grant, the R01. The manuscript topics mesh perfectly with those awarded by the RO3s they support, which include animal-oriented and molecular cellular research. Veterinarians are essential in biomedical research. They not only bring the scientific know-how, but also contribute with their unique expertise and understanding of animal health and welfare to ensure that research is conducted ethically and effectively, leading to advancements in human health. If we ever envision a time when we have in vitro models and computer programs that replace the use of live animals for our research, we need veterinary centers like this one supported by this R13 mechanism. I fully support this concept.

If anything, the number of awards should be increased. Thank you. Thank you, Susan. Dr. Gandhi, would you like to add any comments? Yes, so I think the support of early-stage investigators, especially at this point in history where there's a concern about support of early-stage investigators is the most important thing we could be doing at the NIH. So I really support anything that allows transition from K to R grants. This is somewhat unusual in the sense that R03s are at other institutions, including NHLBI, NIAID, NIAIDM, and NIDDK. But at least to my knowledge at NIAID, it isn't specifically a bridging mechanism from a K to an R. These are $150,000 grants that can be awarded and applied for over two years.

And this seems to be very specifically for the veterinary medicine early stage investigators in during their K Award. I think it's important to say that they can apply even more than once and as long as it's not a no-cost extension the application can occur in that time period, where usually there's a preparation for K to R. This does have a high success rate; these are quote low-hanging fruits or at least usually easier to get in terms of the funding pay lines for RO3s versus RO1s, for example. But I think also importantly what's included here in the modification of this RO3 program is a three times yearly application process possibility where it used to be that it was only possible to apply to these once yearly.

So I think that's a really strong modification to the ORIP CIRCA K01 awardee opportunity presented here. And again, I think it's time, it's certainly, as we look across the universities, we definitely want to support our early stage investigators. This is the time to put out as many initiatives as we can to encourage people to go into NIH-funded research. Thank you. Thank you very much, Monica. If council members have any questions or comments, please raise your hand and you'll be recognized by Francesca or me and asked to unmute yourself. So I think we have a first question. Rafael has the first question. Not a question, just a comment to support this IC in my institution. Francesca or me and asked to unmute yourself. Yeah, I'm unmuted. I think we have a first question. Rafael, what's the first question? Not a question, just a comment to support.

Rafael, we can hear you, and we had this weird echo. I couldn't recognize my voice, but it sounded like it. Okay, all right. So we are good. Rafael, please, your comment. Thank you. Yeah, I just want to very briefly lend my support to this proposal. I see this in my institution where this period is very difficult for our investigators to manage sometimes because there really is no clear mechanism of how to continue to be funded. So, I just wanted to agree with the two discussions that it's a very important thing to continue to support. Thank you. Thank you.

Are there any other comments or possibly questions?

All right, I think we can move on. All right, so well, if there are no other comments, you all heard the motion for a vote on this concept. I think Bettina will type it into chat and I will call for the vote. May I have a motion for approval of the ORIP concept clearance entitled Limited Competition Small Grant Program for ORIP Special Emphasis Award Career, I'm sorry, Special Emphasis Research Career Award circa K01 recipients for an. Is there such a motion? I see so

moved. I see second. Don't even need to ask for this at this point. I will ask. Is there any additional discussion? I don't see any hands and I do not see any comments in the chat. In that case, I will turn the vote over to Christina so she can conduct the vote. Christina. Thank you, Dr. Greeter. The poll should automatically appear on your screen when it is launched. Please remember to hit submit after you've selected your vote. The vote will only count after you hit submit. As a reminder, only council members should participate in the poll. The poll is starting now.

We're not getting anything, at least not me. Is everybody having problems? Yeah, not yet. Yes, we're all having problems getting the poll. There's a second window that pops up, so you might have to just make sure you're seeing all the windows. Yeah, I saw it. Or if you open your chat, it also pops up in your chat window.

It's in the chat. The poll should appear either on your screen as a pop-up or it will appear in the chat.

It's in the chat, but it says the button is disabled. Contact your IT admin for more information. Yeah, it says this bot is disabled. That's what mine says. So I would assume that in the chat they can't vote. They have to have the pop-up window in my screen. The pop-up window is in front of the Teams meeting. And for you, as was discussed, it may be behind. And as a reminder, only council members should participate. We already have 12 votes. It said in mine that something went wrong in the vote. I did hit approve and submitted, but it said something went wrong. This is Barbara talking. Yeah, so let's try something. Let's abandon this whole vote and start over. Because we are actually seeing 12 votes. So 12 of you did vote. Also, I need to remind you, don't vote twice. Only vote once. But so Christina will start over. She will say her same little thing again about the votes. So please, let's start over. Okay, the poll is closing. The old poll is closing. We will open up a new poll. This poll will have a number two next to it. It should appear on your screen when it is launched. Please remember to hit submit in order for your vote to count.

All right, so Christina, this time I can't see it, not that I can, can vote but this time I could not see it, or I can't see it, uh, nor could I and I voted one one moment we are just about to launch it and should launch now, okay. All right, so now I can see it, I hope everybody else can see it as well. Thank you for your patience.

And do you still have the blocking that it says your organization is not allowing this bot? Dr. Bailey, I see you're shaking your head. Yeah, it says the bot is disabled. So I think that might be your university's on your end that they're not allowing that to occur.

This is Barbara. I'm going to log in in a different device. I vote, but it said something went wrong with the vote. So I'm going to try a different device. Okay. Yeah. So let me ask, how many people had the block from their institution or from somewhere else? I see nine responses at this point. And then Barbara said she would log in in a different way. I saw one hand up.

Barbara, Monica. Yep. Okay. So I just, I don't know if we want to discuss it now, but I just opened Teams instead of the browser, and it asked me, do you allow Windows to pop up? And I said, yes. So maybe the next time around I'll be able to see it. So the other version that we can do, we can just vote by raised hands for this concept and then maybe try again for the next concept when people correct it. Will that work for everybody? So we could just ask all those in favor and then you raise your either. Actually, we should give instructions. If you could raise your virtual hands, that would be incredibly helpful. So we have at this point stick and uh okay so now the hands come up I like it so we have at this point raised hands for those in favor and then I will ask those against and then those abstained all right I see 14 hands up and I count those do I see 14 or do I see 13, 15 now Yeah, can you all see how many hands? I want to rely on somebody who counts better than me.

There are 15 raised hands. Fifteen raised hands. I count those as yes. Would you be able to take your hands down at this point? And then I ask for the nose. All hands down. This seems like. Very inefficient way to do it, but all right, all hands down good, so now I ask all those who are against this concept please vote. Not seeing anybody, I'm moving along. Any abstentions? Not seeing anybody either. We go with the 15 yeses. Thank you very much for uh, those votes. Let's hope the next one we can do a little bit more smoothly. With that, back to you, Nicole. Okay, thank you. Just to clarify, the motion as stated has passed. So our next concept clearance for today is a reissue for the Office of Strategic Coordination.

Doctors Trish Loboski and Becky Miller, program leaders in OSC, will present on the concept entitled High Risk, High Reward, or HRHR Research Program. The presentation will be followed by comments from two assigned council member discussants, Dr. Jennifer Manley and Dr. Monica Ghandi. Following the vote, we will move on to a presentation by OSC Director Dr. Carolyn Hutter to discuss a new Council of Councils working group on HR. HR over to you, Trish and Becky. Thanks, good morning. Can everybody hear me? Yes, we can. Oh, good! All right, um, so good morning, and I'm here to talk to you briefly, um, about the renewal. We've had this this program going on for a while, but the renewal of these four high-risk, high-reward notices of funding opportunities, so...

On the next slide, this because i can't yeah right i i can't um advance the slides. And I also can't see the bottom line, but that might be my screen. Anyway, so we're here today to talk about these four initiatives within the NIH Director's High-Risk, High-Reward Research Program. So the four of them are in front of you on the screen. The pioneer, the New Innovator, which is an ESI effort, early stage investigator, the Transformative Research Award that uses an R01, and the Early Independence Award, which is also known as Skip the Postdoc. So we're here to get clearance from you all on the reissuance of these funding opportunities. So the objective of all four of these programs is really to enable important, innovative, **Bold research ideas three of them are very highly focused on the individual, and then the third one, the Transformative Research Program is more project or program experimentally focused.

But really, what we want to do is try to move forward that scientific needle; these have to be bold, these have to be innovative, they have to test or present or hopefully make new scientific

paradigms. So for the funds available, we have listed there almost 60 million dollars per year over the next five years. The anticipation is between 50 to 60 awards per year, and we broke that down, for example, for next year for fiscal year 26, we would guess about five no eight Pioneer Awards, approximately 26 New Innovator Awards, seven Transformative Research Awards, and 13 Early Independence Awards. Each award is five years, but the program is is not being renewed; it's just these funding opportunities.

So our hope today is to vote although I saw how challenging voting is, but vote for approval of the concept for the four notices of funding opportunities listed above. So on the next slide, this is the graphic we use for our four initiatives: Pioneer, New Innovator, Transformative Research, and Early Independence Awards. All of them are designed To foster these incredible scientific leaps, we will take any scientific focus, so anything within the mission of NIH is welcome. This is our, the Commons Fund's investigator-initiated arm. For all four of them, we don't need any preliminary data. We don't require any detailed experimental plan. ALL OF THEM USE RATHER NON-STANDARD APPLICATION FORMATS AND, IMPORTANTLY, REVIEW PROCESSES. FOR EXAMPLE, THE PIONEER INVOLVES AN INTERVIEW WITH THE APPLICANTS. AND ALL OF THEM USE SORT OF AN ESSAY FORMAT INSTEAD OF A RESEARCH STRATEGY. AND WE REALLY WANT THEM TO TELL A STORY OF HOW THEIR PROJECT IS GOING TO MOVE THE SCIENTIFIC NEEDLE. I MENTIONED BEFORE THE HR PROGRAM. Okay,

that was weird. I got a weird echo. The HR/HR program is not subject to the tenure time limit, but each individual award is subject to a five-year limit for the award. So, on the next slide, all four of the goals, all four of the projects, the programs have this similar sort of goal is really as I said to foster these bold scientific leaps forward and the idea is supporting exceptional creativity in the science we want really innovative research so we want the pie-in-the-sky things what we love to hear is when the reviewers say 'I wish I thought of that' or 'this sounds like scientific fiction' if this could happen, this would be amazing. Um, so all of them have to result in bold and highly innovative research, both the new innovator and the early independence awards will support early-stage investigators, the NIH ESI early investigators which is an important part of the program and an important emphasis for NIH.

So on the next slide, I'll go quickly through the four initiatives here. The Pioneer IT'S OPEN TO ALL CAREER STAGES, HOWEVER, USUALLY WE SEE MORE SENIOR INVESTIGATORS THAT COMPETE BETTER FOR THIS. IMPORTANTLY, the research direction must be new, hence the pioneer name, right, has to take up a major portion of their research efforts, at least more than half for the first three years, then it tapers down because these are not renewable. They're highly flexible, so if they are something needs to change within the five years if something doesn't work the investigator is told to work with their program officer and make changes so again we make approximately seven of those a year. The next slide: the new innovator award. This is the first one that supports early stage investigators.

Again, it must be highly innovative; it's in the title that's what I tell applicants all the time: we want the innovation to be off the scale, at the same time reviewers do focus at least a little bit on feasibility so they're not crazy innovation, they're doable. So it's similar to the Pioneer in spirit,

but again it's only early stage investigators. For those of you who don't remember, that's an individual that's within 10 years of their terminal doctorate, their PhD or their clinical residency if they're an MD and they must not have received a large independent NIH grant yet. So they need to focus 24/ 25 of their research effort, and again, they had the the the review and the the essay has to focus on the idea innovation potential impact, the history, the track.

record of innovation for the pi and then of course why this should be a new innovator award and not an r01 the next award the transformative re on the next slide the transformative research award we actually do use an r01 mechanism a more traditional mechanism but we use it very differently this award different from all the others could support a project that might be a team approach you could also be a single PI but you could have a team here the budget is flexible it's not fixed it has to be very well justified but it's not fixed at a certain amount there's a little bit more emphasis here on the project versus on just the PI. The PI, of course, has to be stellar, but they're really, the reviewers are told to look at the project.

Again, there's still, you do not need preliminary data. You don't need a detailed experimental plan. So the last one, the fourth one is the, and next slide, is the NIH Director's Early Independence Award, right? So these are individuals that are skipping their traditional postdoc, and it's for a really special group of students that are graduating. And the time window is pretty tight. I won't go into it here, but it's about a year within the time of the application. But they have to really have demonstrated an incredible track record of what they've done in the past. The other thing that's important is that the institution supporting the application, who's the real applicant, must give a demonstration of really substantial support, commitments monetary, commitments space etc to that individual; they will if they receive an award, the PI will commit 80% effort and they must have that available research effort time that they can give so on the next slide.

Just a little taste. I really can't give you all the impact that these awards have made over the many years, but you can go to our website and this is just a snapshot of some of the recent highlights that we've put out there that have been really important. So we have areas of research and Alzheimer's disease, kidney disease. Yeah, microbiome, gut inflammation, and then the last one there is development of language. So we chose these because they're most recent, but also to give you an idea of how broad the scientific areas are. With the HRHR program, we really aim to hit the whole scientific enterprise of NIH and that's highlighted on the next slide, which is the working group that I work with.

Work very closely with some of these names have changed very recently, but you can see if you wanted to, all 27 institutes and centers are represented here. These individuals pitch in; they really are wonderful group, but this is part of why we can look at the entire research enterprise. So on the next slide, I believe it's... yeah, I tossed this back to you, Francisca. Or questions? I don't remember. Thank you very much. So actually, we'll now go to our assigned discussants. Hopefully, we have the audio issues worked out for Dr. Manley. Dr. Manley, do you have any? I hope so, too. Oh, yes. Great. We can hear you. You can hear me. Okay. Well, I'll introduce myself then quickly. I'm a professor in the neurology department at Columbia University, and I

was previously on the NIA, the Council on Aging. And I'm very happy to be discussing the high-risk, high-reward program today. You know, the advantages and successes are many. The existence of a program that focuses on encouraging creativity and innovation in NIH research.

Dr. Manley, unfortunately, we have lost your audio. Just give it a moment and see if we can regain. Can you hear me? We can hear you now. It seems to be cutting in and out. I would suggest if that happens again, maybe try turning off your camera to save bandwidth, but please go ahead. Okay. The as I was saying, the support for early stage investigators for two out of four of these awards and the broad impact across the NIH are all advantages. I had some questions, though, and specifically the questions are. what are the specific metrics of success for the high risk high reward program in the materials given we were given a snapshot you just talked about it I followed the link a lot of different grants are represented after you follow that link and so it was hard to identify exactly which of those news stories.

Sorry, Dr. Manley, we have lost you again. I would suggest at this stage trying to turn off video to save bandwidth, and then hopefully we can get your audio back. Yep. Okay, we can hear you now. Yes. So what are some of the what's some of the evidence that the folks who are awarded high-risk, high-reward awards are indeed bold and highly innovative research? Would some of the evidence be high-impact publications, novel discoveries, life-changing treatments? What is some of the evidence that these high-risk, high-reward programs engage scientists across all of the NIH institutes and all of the disciplines that are represented in NIH? All of the signs that we have now point to the future budget of NIH to be drastically reduced. How do we view the role of high risk, high reward programs in the context of drastically reduced resources?

For example, should the high risk, high reward program be even more focused on early career researchers given the funding environment that we're about to enter? And then I ask, what are the specific outcomes of the Early Independence Award? This is the one that allows for postdoc to be skipped. We want these scientists to be successful, but what is the evidence that they are successful in obtaining R01 awards and promotion to associate or promotion to tenure? And those are my comments. Sorry about the audio issues. Okay, um, I can have a lot of questions there, but I can try to answer some of these, um, the metrics of success, some of them are ones that you cited that you might imagine, things like follow-on funding especially for the ESI programs, the new innovators and the early stage, early independence award.

Follow-on funding is a huge metric of success often its tenure often comes to these folks a little bit further out, so I'm not sure that we have those data. We have it for DP2s, for the new innovators, but not early independence awardees, although in a minute, Becky, I'm going to hand it over to you to talk about that. Warning for pioneers and transformative research awards obviously one of the metrics of success would be important papers and impact in the field that those papers are used; we often use relative citation ratio to figure out that papers aren't just published and ignored, that they're actually cited and built on, so again this takes time-you can't measure that you know, two or three years after the end of the award.

It takes a little while, but that's another way that we look at these. In fact, we're right in the middle now of doing an internal evaluation for the top 10 findings from the HRHR program. That's one of the things that I really want to be able to articulate very clearly. The evidence for impact across all the institutes and centers, I showed you the list of folks that are working on the program. And the way most of these awards work, everything other than the Early Independence Awards, although it's Office of the Director funds, they're administered out there in one of the other 26 institutes or centers, okay? So they're moved out to NCI or NHLBI or wherever.

And that's really an important aspect of the program, and that's how we can sort of measure that we are hitting all of the institutes and centers at NIH, and that all of the institutes and centers at NIH are very eager to take these on. And we place them where they're most scientifically relevant. I would, I don't have the data at my fingertips, but we would have to pull that up for you. But I assure you that some of the smaller institutes and centers are well represented in our portfolio. I can't really comment on the role of HRHR research in the NIH budget. I think that'll be a question you can ask some of the other NIH leaders that are coming on later today. I don't think that's something I can comment on.

Becky, do you want to talk just a little bit about the success of the Early Investigator Award recipients? Yeah, so for all four initiatives in our program, we've had a third-party evaluator look at them to actually chart to see how well we are doing in our goal of successfully supporting high-risk research. And for all of those, they actually did, they compared our cohorts with a matched R01 pool to look at outputs and view whether or not we are in fact seeing more innovative science out of our group, and there's a lot of details to that. But in general, for all four initiatives, those results the evaluator did find that we were successfully able to support high-risk science. So, a lot of those evaluations that are on our website, you're welcome to go look through them.

But in general, they have found that we are able to support and are finding those high-risk projects. For the Early Independence Award, we also had a third-party evaluation conducted on it. They did a matched R01 pool. As you can imagine, it was really hard to find a really good comparison group for these batch of very ambitious and mature scientists just coming right out of grad school. So they used ESI R01 and they were able to conduct surveys. They looked at things like career advancements, so when did you get tenure, what were your research outputs, follow-on funding, all that information. And they found that the early independence awardees were able to They matched the ESI R01 comparison pool in terms of length of time for tenure, their research outputs, and all of that.

And they were able to do all this after skipping additional training. So we felt that was a great success for the Early Independence Award. I want to mention, I didn't say this, that the Early Independence Awards are managed directly by Becky. She is the program officer for all of those awards. She goes on site visits, meets with PIs, meets with the institutions to make sure that the goals of the program are supported and that those PIs have the support that was promised to them in the application because that's a huge part of this. The institutional support matters a lot.

I agree. Thank you for your answers. Thank you all. Now I'll turn it over to Dr. Gandhi to add any comments. So, I mean, I highly support all four of these.

The recent events have created a chilling effect for researchers, the extramural researchers at the NIH, both early stage and late stage. Later stage investigators and what would be great to help in terms of getting on track is to focus on actually not just the early stage, but to think about the transformative research awards and pioneer awards in terms of being at any career stage. I think that if we take those two separately, one is essentially pioneer award as person-based, and the other transformative research award is project-based. And what I think really needed right now is an idea that you can help, you know, with given terminated grants and other concerns that have been really difficult for current extramural researchers, figure out if there could be an expansion of this program to get more people sort of in a project-based way for the transformative and pioneer for the person-based help.

Get back on track with funding. So I would certainly support this, but beyond support this, hope that there is maybe even expansion of those two particular ones. With the K awards, with the early stage investigators, DP2s have been incredible to kind of go. It does take away your early career status to get a DP2, but you get $300,000 a year, which is kind of in between. It's essentially not as much as $500,000 a year for an R01, but we have several people with DP2s and they're great awards. But I would focus, if we can, right now on any career stage awards and maybe enhance those to kind of help people with what's happening right now. Thank you. Yeah, thank you. That's a very important observation.

After the vote, our office director is going to talk about some, well, you'll see some maybe potential new ideas for expanding the HRHR efforts in our group. Yeah. Thank you. Great. Thank you. We'll turn it over to other council members for questions or comments. And I see some hands already being raised. So, Francesca, can you? Yeah. So, I see, Rhonda, your hand is up. Why don't I go to you first for your question or comment? Thank you so much. So, thank you so much for this presentation. Certainly, this is one of the hallmarks of NIH innovation, and really being able to promote creativity in this way. I just have a couple of questions, and part of it is on what Dr. Manley brought up in terms of metrics to show success.

Given the environment, and particularly with cuts to NIH, are there any considerations as it relates to the areas in which individuals plan to research in? And I bring that up from the standpoint of you, certainly scientifically relevant was the term used, but also a high-risk science too. I'd like to bring another consideration here, and that is the areas within our healthcare delivery system where there's a need for new innovative ways of approaching. And let me give a simple example of one from India, where the Wish Foundation actually funded, put out RFIs, I guess you could call them, or grants for innovators to come up with a way to do mammograms successfully, but at a lower cost, since it is a screening mechanism that can be more applicable if it's something that's more affordable.

So, I'm just wondering whether or not there are other considerations or themes that will be introduced in the decisions of which things go forward, recognizing that we're in a situation

where budgets are very important, being able to be cost-effective, as well as scientifically effective. Thank you. Jomana Musmar-Yeah, thank you. That's a good question. As I mentioned, we invite all research from across the NIH mission space, and obviously the areas you're citing are within the NIH mission, and they would be encouraged to apply. I can't tell you how many emails I get asking whether this area or that area is eligible, and the answer is almost always yes, it's eligible. So they're always eligible to apply. The critical thing for us is they must fare well in peer review.

So if it's an out there idea on an area we would like to support, but they don't do well in peer review, we can't do anything about that really. So we keep it open. We don't specify, you know, we would like to have maybe healthcare delivery. Areas of research emphasize. We have not done that. There are other efforts across the ICs in more specific areas of research, by the way, that do that. But I'm just talking about our program. The other thing that's important to note is if the applications receive a score they go through a process called programmatic priority review and that is written out in the funding opportunity one of the things that we can emphasize is if the area of science is outside what we've funded a lot in the past, for example.

And if there is something that receives a score that maybe is on the border between lines of funding or not, but it's something we've never seen before and we note and the reviewers note that this is going to make a huge impact, we can support things like that. So I think that's an important aspect of how we try to spread the funding to really cover every area of science that is peer-reviewed favorably. But that peer review is important. And I'll tell you that, you know, that's what your peers that are doing that review. So we are beholden to that at least a little bit. Does that answer your question? Yes, it has. Thank you so much. I appreciate your response.

Okay great thank you very much I see three more questions or three more hands and therefore let's go with them so Rafael you are first followed by Ross and then Jen thank you I am fully supportive of this I think there should be even more funding for these kinds of initiatives compared to some of the other research that is funded by the NIH my question is if any institution, if every institutional research institution is going to be is this going to be available to all research institutions and if not what are the criteria to exclude them and how will they know in advance so that we can't apply not spend time applying oh I'm sorry I didn't make that clear earlier. This is open to all eligible institutions.

So, any institution that can apply for R01s, that they would be eligible. Yeah, there's no limitations on that. Jomana Musmar-Great. Thank you, Pat. Ross? Ross Cohn-Great. Thank you. I'm also very supportive of these programs. Both in the last concept clearance and this one, the question has come up as to how we measure success and what those key performance indicators are. We have a natural experiment, which is that you have many individuals who apply for these awards and are not granted them. And in particular, you know, study section is ranking these applications and there's a cutoff line, there's some funding line. And the folks who are just below and just above that funding line sort of make a natural experiment to say what would happen if you didn't have support of this program.

Is there any consideration instead of just, you know, listing the accomplishments of the awardees, particularly for those early career awards, of actually asking how did their career trajectories compare with those who did not; who were not awarded these particular mechanisms. Well, as Becky outlined better than I, what we've done in the past is compared our award recipients to R01 award recipients. Now, I've never gone through and looked at whether or not the people that are on that line received an R01 in the same competition year, if they exist, I think that would be very few. I don't think it's fair to compare awardees and non-awardees if those non-awardees didn't get any funding, right? I think we know what might happen to them. We can do that, I suppose.

That wouldn't be hard, but we have not. I don't know, Becky, do you want to add in on that? We did look at those who were scored but were not ultimately funded. For the pioneer evaluation um but we haven't we there were problems with that comparison so in the future when we look to other initiatives we opted not to use that pool as the comparator just because um it wasn't deemed a fair comparison yeah i mean it's it as others have mentioned if we're going into an austere period of funding demonstrating value, right, for the existing funding mechanisms is going to become even more important. And, you know, there's a little bit of an intrinsic bias here that your most outstanding candidates are likely to win these awards, and they're most likely to succeed in any case.

And so, to some extent, I think, to the extent that we can demonstrate the true value of these mechanisms to a broad audience, I think that's going to be essential. It's an interesting idea. I'll take that back and we'll think about it. I don't think that was the bias I was intending to communicate. My point was that it's not really fair to compare a group that received funds and one that did not receive funds. I think, you know, a little common sense knows that that's going to impact their career. But I like what you're saying, and we'll take that back and think about it. Thank you. Great. Thank you. So we'll go last to

Jen. And then a short answer maybe okay so uh this is a a quick comment and a question so the comment is uh you got a question earlier about whether the awards are available for all institutions and I'm also uh sure that um the intention is to support science that supports uh or that would provide uh help for all Americans. So on a quick search of the of the tags list, which are canceled grants over the weekend, I found that five of these awards, at least five have been canceled recently of the high-risk, high-reward programs. And so that's my comment. My question is, just like Raphael asked, whether the awards will be. Available to all institutions, will the awards be available to all topics, all scientific topics? So, as I stated before, they're open to everything within the NIH mission space. If there are areas of science that by NIH policy we are not going to support, then those probably will not be supported.

Okay, thank you. Sorry. All right. So with that comment, I think we can move on to the vote on this concept. And then, as already alluded to, Caroline Hutter will follow with a discussion to the future. We discussed on our end how we should do the vote. We are going to continue with this hand-raising method because we believe that is a better outcome. And let me first call for the motion, and then I'll hand it over to Christina for the actual vote. May I have a motion for

approval of the Office of Science OOSC concept clearance entitled High Risk, High Reward HRHR Research Program? Is there such a motion? I see so moved. I see second. Thank you very much. Is there any more discussion at this point?

I see no more raised hands. I see nothing in the chat. With that, I'll turn it over to Christina. No, I was voting. Sorry. Never mind. I was voting. It's always good to have multiple eyes looking. Christina, please go ahead. Thank you, Dr. Greeter. As mentioned, this is a vote for approval of the OSC consum clearance titled 'uh high risk high reward research program please raise your hand to vote 'I' for the presented concept, thank you. I see 15 raised hands. Please lower your hands and we will move on to the next vote. Please lower your hands. I see thank you. Please raise your hand to vote 'nay' for the presented concept, thank you. I do not see any raised hands. Moving along, please lower your hands if they were raised. Moving along, please raise your hand to vote 'abstention' for the presented concept.

Not seeing any raised hands, the motion as stated has passed. Thank you. Thank you, Christina. Nicole? Thank you all. Okay, moving to the next section. So one of NIH's and especially Deepak Ipsi's key goals is to foster fundamental creative discoveries and innovative research strategies. So achieving this requires a range of approaches, including identifying and supporting research that has the potential to disrupt current biomedical paradigms and open new pathways for disease prevention, diagnosis, and treatment. So this transformative research often includes creative approaches and substantial breakthroughs that challenge norms and arise from novel ideas on the edges or intersections of disciplines. So transformative research inherently involves a level of risk and uncertainty, and also has the potential for exceptionally high impact.

So, as a result, these high-risk, high-reward initiatives that allow for increased innovation and experimentation can ideally lead to groundbreaking discoveries, address challenging questions, and catalyze scientific progress. So, there is opportunity for Deepak Ipsy to build on the success of the programs, such as those that you just heard about. And we are trying to examine additional ways that Deepak FC could advance novel approaches and outcomes, working in partnership across all of our NIH institutes, centers, and offices. So we think that there is space for more strategic opportunities targeted on how we can improve and expand on our existing efforts. So we have a proposal on how we might do that, which we would certainly appreciate your thoughts on. And Carolyn will elaborate further. So with that, Carolyn, the floor is yours.

Thank you. And thank you, everybody, for joining us this morning. I'm very excited that we were able to have this Council of Councils meeting scheduled. So, again, for those of you who don't know me, I'm the Office Director for the Office of Strategic Coordination. And what I'm presenting today is a proposal for an HRHR working group of the Council of Councils. And if you go to the next slide, please. We're wanting to focus this on transformational biomedical research. And I will say that the discussion that you all just had after Trish and Becky's presentation really sets the stage for why we think a working group in this area at this time would be important. As Nicole just laid out, you know, we wanted this working group would be broader than an analysis of the existing HR-HR programs, and really look at

how do we think about innovative research that goes beyond incremental advances and creative approaches in this space, and really come after the challenges about how do we identify critical topics and approaches with potential impact, how do we develop appropriate mechanisms and review processes, and building on the discussion we just had, and certainly part of our consideration in thinking about this working group, although not listed on this slide. Slide is also how do we evaluate success, what are the appropriate metrics and the the ways to sort of study when are when are we having success and what opportunities lead to success in this area? Next slide, so as we think of a working group of this council, what we would hope that we would be able to come together with a group to discuss is how do we best foster transformative biomedical research, not just in the deep Poughkeepsie but across NIH.

What's the appropriate portfolio balance for these types of efforts? Like I just heard some of the feedback that maybe we should think about increasing what portion of our portfolio goes to these types of efforts. How do we assess that? How do we assess whether we're taking appropriate risk? How do we assess whether we're having appropriate success? How do we broaden the participation? Again, really, you guys set the stage with these kinds of thoughts with the questions you were asking about ensuring that we're hitting all of the institutions, that we're hitting all of the scientific disciplines, and really covering the full translational science spectrum, not just in a basic science area, but all the way through to implementation science and other areas.

And what's the appropriate way for Deepa Kipsi to take a leadership role in this space that would have an impact on not just things within our division but within NIH as a whole. And so with those slides sort of as background to let you know what we're thinking in this space, we just wanted to open it for a discussion a little bit to hear from you all about whether or not you're supportive of our pursuing a working group in this area, and then also if there's questions in addition to these sort of open questions that we've outlined here that you think such a working group should pursue. So you can pull the slides down, and I'm happy to take feedback and discussion. And I see Kevin already has his hand up.

Thanks so much, Carolyn. Yeah, let's open it up for questions, comments, discussion. Kevin, please go ahead. Yeah, hi. Thank you so much. I wasn't going to say anything, of course, before this, but I have been the beneficiary of OneDP1. And so I'm doing work in the space of AI and primary care. If I were staying on the council, I would definitely be wanting to be a part of this working group. So I'm happy even off the council, if people need someone to chat with about it, I'm happy to participate. Yeah, and I should say that these working groups include both internal and external to council members. Okay, well, then maybe I'll do it. But in fact, I will do it. No, I think it's a really terrific idea.

I think both the conversation about metrics, because the world has changed, and some of the metrics you might choose to use are very different. I actually had thought at one point about a really interesting hurdle for pioneer awardees, who are especially more senior people, to overcome before applying. And I'd love to chat with the working group about that idea. I think I

was looking, I was trying to capture that slide, Carolyn, that you had up that I just didn't capture in time to answer the exact questions. But I'm very supportive, and I think that getting a working group involved, especially given, and I won't call them austerity measures, but given what's happened recently at the NIH, I think it would be very useful for us to have a conversation about what this program can offer in addition to whatever the overarching ecosystem is for training.

Training and high-risk high-reward work are great. Thank you very much, Kevin. Um, so next I see Rhonda with her hand raised, please go ahead. Thank you. Um, I find this to be very fascinating, but a question I have for you, I, I realize that most of the participants are from NIH in the various divisions. Is there any thought about including others who are major stakeholders in healthcare in general in this? Because it can bring a different perspective or a different need. So, let me give an example. Certainly, the CDC cites chronic illnesses, particularly those at high prevalence, those that have a high propensity for death. But one of the things they are not necessarily looking at at this point and probably are not aware of are those conditions that are increasing in trend where the ability to identify them or to treat them becomes kind of a real great trial and error procedure.

I say that to say because trial and error wastes time, but also wastes time. money as it relates to accomplishing what needs to be accomplished. And autoimmune diseases is probably a prime example of that, which has increased in prevalence and seems to have quite a few different conditions attached to that. So that is one question. So I'm wondering whether or not there would be some input to this group in terms of what are some of the real-world issues that are being dealt with by those who are taking on the responsibility of populations, not only from a health outcome perspective, but also from what I would call monetary responsibility. So, for example, employers who are self-funded, health plans, provider groups that are now taking on accountable being accountable for the populations that they're servicing.

So, someone gets ill, they have to really help that population get better in that regard, and they've got to do it within a certain window of dollars, which I think we all are realizing are becoming less and less. So, I'm just wondering, is there any thought about external stakeholders having some input, not necessarily on the council, but having some input as being a very important part of the discussion. Yes, Rhonda, and I should clarify the working group membership that Trish shared previously, that's the group within NIH who oversees the HRHR programs. Oh, I seem to be freezing a little bit. I will also turn my camera off. Um, so that oversees the HR HR programs that we administer and that's separate from the working group we're talking about right now, and a hundred percent the working group that we're proposing right now would entirely have external people, and as we've been developing a potential roster, we've been considering not just people in sort of academic and traditional funding expertise, but also additional broader stakeholders.

And so I hear you in making sure that we're sort of representing the healthcare and innovation in the considerations about what we need to be doing in healthcare as one of the key stakeholders that we could bring into this working group. And this is a great opportunity, actually, to get that type of external feedback into the NIH process. That's part of the reason to have a group like

this. Thank you. Thank you for that excellent feedback. Jean, I see you as the next person. And to support what Rhonda just said, I think that's really interesting. I was really also thinking about stakeholders. But to go back to as we decide on what that working group should look like, when I think about how we decide what's a critical topic.

I feel that's going to be probably the most important thing as we set up the working groups. How do we define a critical topic? A critical topic for you may be different from me. I think about is it the impact it has? Like rare diseases may not have the same impact in terms of numbers, but very obviously critical for many people who have those rare diseases. It's probably an outside-of-the-box kind of conversation, but that's what I'm trying to say. Like, how do we define that? What are the metrics we're going to use? And hoping that the working group sorts of approaches it that way. When I think about interdisciplinary and being at the cross-section of different things, in that space, I think about collaborations, bringing together different groups.

What do we define as a collaboration that could work? What does that look like? What are we trying to find? In there, I think about stakeholders like industry partnerships. So I don't think it necessarily is academic to academic. It might be interesting to have academic with industry where we have identified something that is of critical importance. Because for me, when we do the high-risk reward kind of areas, sometimes there's no sustainability in them. So we do them, they get the grant, they do whatever it is they're going to do, and we don't have resources to follow up. So high risk, high reward is fabulous, but then you have to go from reward to actually implementation. And that is different. And how are we going to look at that?

And how are we going to propose to get from point A to point B? So broadening participation is the last thing I want to talk about. When we talk about broadening participation, and me again, it's people from different walks of life, different places. different diversity portfolios. And I really want us to be very thoughtful and deliberate and diligent about what we mean by broadening participation. So those are my two cents. Yeah, no, excellent feedback. And again, you guys are all just highlighting for me through your discussion, even more enthusiasm for having this working group and the key types of challenges and thoughts that we should be bringing forward and giving good consideration. Exactly. Okay, great. I think the last person who had their hand raised for comment is Kent.

Kent, would you like to go ahead? Yeah, thanks, Dr. Kloscher. Carolyn, Kent Lloyd, UC Davis, good to see you again. Good to see you, Kent. Just a point of clarification on the boundaries of what the working group is to work within. So is it a matter of, is it primarily a review of how the HR, HR programs are now and maybe how to modify and tweak them to be more transformative? Or is it looking at a wholesale restructuring and maybe, you know, throwing out the old and building something new? What's the boundaries that you're going to want the working group to operate within? Right. I mean, I don't want it to be an evaluation of the existing HR-HR programs. As Trish and Becky highlighted, we already do that as part of our normal evaluation.

Okay, I'm turning my camera off. Within the Common Fund. So, really, the goal is to think about transformative research at NIH, not just funded through OSC and DPPC, but NIH broadly, and make sure and think about are we on what else can NIH be doing what's a forward look at things that NIH can and should be doing in this space hopefully complementing rather than replacing our existing HR HR efforts um but obviously there may be some impact on our existing HR HR efforts but it's really much more of a forward-looking what what more should we be doing rather than a direct evaluation of the existing programs does that make sense? Yes. Okay. Thank you very much. Thanks.

And I think just to sort of recap some of the feedback that we got, highlighting sort of the need to include external individuals from healthcare and other industries will really provide us with that range of scientific expertise to ensure that we are meeting the goals that Carolyn just laid out in terms of really pushing the boundaries and being transformative in our HR portfolio. Okay, I think that that brings our morning session to a close, our open session to a close. We're doing very well on time; we're 10 minutes ahead of schedule, so we get a slightly longer break. So we're going to take a short break before we transition to the closed session of today's meeting. So I'm going to ask all of our council members to remain logged in and muted.

We will see everyone back at 12:15 p.m. ONLY COUNCIL MEMBERS AND NIH STAFF WITH A NEED TO KNOW WILL BE PARTICIPATING IN THE CLOSED SESSION. FOR EVERYONE ELSE, THE OPEN SESSION WILL RESUME AT 1: 15 PM. THANK YOU ALL. WELCOME BACK, EVERYONE. WE ARE RESUMING OPEN SESSION. NOW IT IS MY GREAT HONOR AND PRIVILEGE TO INTRODUCE OUR NEXT SPEAKER, DR. JAY BHATTACHARYA, THE 18TH DIRECTOR OF THE NATIONAL INSTITUTES OF HEALTH. President Trump nominated Dr. Bhattacharya for the position on November 26, 2024, and the U. S. Senate confirmed him on March 25, 2025. As director, Dr. Bhattacharya is overseeing the nation's premier medical research agency. Dr. Bhattacharya will play an instrumental role in shaping the agency's activities and outlook, ensuring they align with the President's Make America Healthy Again Commission.

A renowned doctor, researcher, and health economist, Dr. Bhattacharya held a tenured professorship in the medical school at Stanford University in California. Dr. Bhattacharya's research has focused on population aging and chronic disease, particularly on the health and well-being of vulnerable populations. Encouraging different perspectives will be central to Dr. Bhattacharya's approach to leading NIH as part of his larger mission to restore public trust in science. Alongside Secretary Kennedy, he will champion innovative, cutting-edge research that fuels near-term solutions for patients while balancing investments in basic science. Dr. Bhattacharya earned his bachelor's and master's degrees in economics from Stanford University. He then completed medical school and earned a PhD in economics, also from Stanford University. Dr. Bhattacharya, the floor is yours.

We can't hear. Okay, can you hear me now? Yes, we can. Okay. Yeah, I'm absolutely delighted that I've had the chance to lead the NIH at this time. Next slide, please. Next slide. Next. So, for this talk, what I thought I'd do is I would talk a little bit about background. Nicole mentioned

some of it, but I just wanted to emphasize a couple of points about it. In particular, my love for the NIH and for the mission of the NIH and my absolute commitment to make sure that the NIH continues to be the crown jewel of research, biomedical research in the whole world. I'll talk a little bit about the leadership transition and other changes. In particular, I'll focus on some of the the early initiatives that I've worked on that I hope we can get that will make the research community have availability to data and other access to research resources that they didn't previously have access to, as well as an initiative on the etiology of Alzheimer's and its various manifestations.

And finally, I'll end with my vision for the NIH. Next slide, please. So, Nicole mentioned that I came from Stanford. In fact, I was at Stanford for almost 39 years. So, my entire outlook is rooted in the biomedical community where Stanford has played such an important role. But I should also mention that the NIH has played a tremendously important role in my own in my own development. I've been a NIH-funded researcher my entire career. I've served on NIH study sections. I've worked very closely with NIH officials in many, many different projects before I became the NIH director. And I love the NIH. It's, to me, an institution that I'm absolutely committed to making serve the American people.

The mission of the NIH is absolutely the core of my research agenda as well, research aimed at improving the health, longevity, and well-being of the American people, that is a mission I think that we all can agree on. And it's that vision I want to, that mission I want to make better while I'm the director of the NIH. Next slide, please. Okay, so first some leadership transitions. I should mention First, Nicole Kleinstreyer, she is joining us as the head of the director for DP KIPC. She was previously the director of National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods. There are many leadership transitions happening, and in particular, the leadership of the institutes. I'm committed to a normal process to replace the people that have left and retired.

This time of transition is, I recognize and I've heard from so many of my colleagues and friends, a time of anxiety and change. But I want to make sure that everyone understands that although every inch of the federal government is under scrutiny, and of course the NIH is not exempt; the mission of the NIH will continue. As we navigate these challenges, I will do my best to lead the NIH with reforms and implement new policies that endeavor to earn your trust and the trust of the scientific community. At the end of this, the NIH will be a stronger institution that fosters scientific discussion and debate and advances in new technologies, new ways of thinking that meet the mission better than we currently are. So, next slide, please.

Let me talk a little bit about a few a few early early initiatives that I've worked on. So first is an initiative requested by the President of the United States to Secretary Kennedy and then transmitted to me to have a, to initiate a research program so that we have a better understanding of the etiology of the autism spectrum disorders as well as associated conditions. To do this, the NIH is launching an initiative inside the Office of the Director, where the goal is to integrate diverse data, enabling researchers to examine complex factors influencing the rapid

rise in autism spectrum disorder. In 2022, the MMWR, the CDC, estimated that one in 31 children had some form of autism spectrum disorder, a very sharp increase from previous years.

Autism spectrum disorder is a highly heterogeneous condition with many potential causes. And understanding its ideology is absolutely crucial to developing treatments for the range of conditions that this disorder represents. The NIH is committed to identifying causes, risk factors, and treatments through investments in research programs, coordination of interagency activities, and collaboration with the autism community. To this end, we're launching an initiative to accelerate the understanding of causes and improvements in treatment. This new initiative will leverage large-scale existing data resources as well as data resources that are available throughout the rest of the federal government as well as in the private sector. If needed, researchers can generate new data that will link to these and openly query contributions, contributors, risk factors, and causes of autism.

To do this, we will use a rapid timeline of a large grant process that will be run through the Office of the Director. WE WILL SUBJECT THE EXTERMINAL RESEARCHERS WHO APPLY WILL BE SUBJECT TO NORMAL REVIEW PROCESSES AND HAVE ACCESS TO THE DATA RESOURCES, WHICH I'LL MENTION IN JUST A SECOND. The idea would be that somewhere between 10 to 20 groups of researchers from across the country, again, run through normal NIH processes would be able to ask questions ranging, using methods ranging from basic science to epidemiological approaches to other more applied approaches to ask what causes autism and how best can we treat and manage autism so that so many millions of families have an easier time dealing with the problems caused by having an autistic child. Next slide, please.

I recognize, of course, that autism is a range of manifestations ranging from highly functioning children to children that are quite severely disabled. And, of course, the research will account very carefully for those distinctions, the highest quality proposals. To make this happen, what we're going to do with the NIH is launch a real-world data platform. The idea of the platform is that the existing data data resources are often fragmented and difficult to obtain. The NIH itself will often pay multiple times for the same data resource. Even data resources that are within the federal government are difficult to obtain and use by researchers. So, what we're proposing is a transformative real-world data initiative which aims to provide a robust and secure computational data platform for chronic disease and autism research.

This data platform, though, will be unveiled and used for the autism issue I mentioned earlier; it will also be available for other research programs within the NIH on chronic disease and other topics. The platform will facilitate collaboration across the Department of Health and Human Services and fellow government entities more broadly to establish a comprehensive launch of health data sets with broad coverage in the U. S. population. This will include claims data for Medicare, Medicaid. We're working on a memorandum of understanding (MOU) with CMS to establish broader data use agreements within the NIH for that purpose. It'll include electronic health record data from the private sector, and it'll include other claims records. It'll include existing data resources, such as the genetics data that the NIH has, as well as toxicology data

and environmental exposure data from across the government and private resources, including private industry.

Many leaders in the data science space have contributed to this strategy from DPC/ KIPC offices, programs, and across the ICs. And so this platform will feature the cutting-edge knowledge that the NIH already has. If you look in this figure, you can see that the platform will integrate and link data from real-world sources, such as pharmacy chains, so that you have medication records, health organizations, including the VA, Defense Health Agency, Indian Health Services, clinical data, as I already mentioned, electronic health records, so you have access to labs, imaging, genomics, claims and billing data, which often provides detailed diagnostic information, as well as information about the use of occupational health. Health and other resources, environmental data, air pollution, environmental toxins, as well as some data on sensors and wearables like smart watches and fitness trackers.

By bringing these data together in one place, providing access to advanced computation resources, and leveraging the latest techniques, the AI techniques, the platform will accelerate research and create new opportunities for cross-agency use of data in real-time health monitoring, developing national disease registries, including a new one for autism, enabling faster drug development, enabling longitudinal data sets to better understand the progression of disease, and launching national competitions, as well as research programs for innovative and cutting-edge research to answer key questions such as the one on the etiology of autism. The real-world data platform will preserve the privacy of patients, sort of within the context of the platform itself. Researchers will be able to do their work on the platforms but not be able to download the data themselves.

And there are state-of-the-art protections to make sure that although linkages across the datasets will be permitted inside the platform, that these linkages do not in any way threaten or the confidentiality of patients. Next slide, please. To do this, we will form collaborative partnerships with federal, state, and private entities to expand data resources and identify opportunities. The platform development will leverage existing programs as a foundation, such as the Healthy Baby Child Development Program, the National Institute of Aging Linkage Program, which currently links NIA-supported study data and CMS claims data, and the NCATS N3C platform, which systematically collects data derived from chronic health records from different institutions and harmonizes these data into data enclaves. We'll use all available funding mechanisms to build new partnerships and research opportunities.

The strategic approach will enable an agile implementation; engagement with non-traditional research partners and support NIH-wide development to drive platform growth. I've already reached out across HHS, including to CMS and other entities within HHS, as well as in the NIH itself, and have had nothing but enthusiasm for participation in this. We've had a great conversation with some of the folks in military health who are also quite eager to get these data in the hands of researchers so that we can ask questions, again, not just about autism, but about a whole range of conditions that would benefit from close analysis of these data by expert

researchers in the extramural community. The project will have predefined milestones and checkpoints, ensuring efficient operation.

But the key thing is that we will We will make sure that the processes inside to obtain and use these data inside the new real-world data platform guarantee patient safety, protection of patient confidentiality, so that while research access will be easy, harming patients as far as their confidentiality is concerned will not be possible. Next slide, please. Okay, last bit of my talk. I want to talk about five major aims I would like to accomplish as NIH director. And let me just put this as a blueprint for the future of biomedical research because I think the NIH can play a tremendously important role in shaping what the next century of biomedical research will look like. Next slide, please.

So first, and you can probably tell from the time I spent on the autism study and on the Real Data platform, the NIH absolutely must address the must address the key health needs of the country. Since 2012, the United States has had flat life expectancy. In a sense, the key mission of the NIH, one of them, which is to expand longevity of the American people, has not been achieved. And with the pandemic, the life expectancy collapsed even further, and only recently has it come back up to 2019 levels. Chronic disease problems, including obesity, diabetes, heart disease, I can go through the whole litany, are so prevalent, inflicting the lives of millions and millions of Americans. The Make America Healthy Again idea is something that's basically uniformly popular.

And the NIH must play a role in making sure that we focus on those diseases that most afflict the American people so that we can improve their health and address the needs that they have. The kinds of approaches we have will aim at not just at the cutting-edge research that produces expensive new treatments, but also scaling and making more accessible, new findings that will be available to the whole of the American people, not just a part. We have to find better ways to prevent, treat, and cure chronic diseases. Our research is not simply focused on how to manage late-stage chronic disease, but also on how best to prevent the development of chronic disease and then the complications of chronic disease once it's in the early stages, and if we can find cures to do that as well.

Next slide, please. The second goal that I have as NIH director is to solve the reproducibility crisis that has afflicted science for decades now. In the early 2000s, my Stanford colleague, John Ioannidis, wrote a very famous paper where he documented in very simple ways that large chunks of the scientific literature simply were not replicable. The replication crisis that ensued in field after field has undermined the confidence that the public at large has in the biomedical enterprise. And during the COVID-19 epidemic, this became very, very severe. This problem became very, very severe with the suppression of ability for people to dissent against scientific dogma and the elevation of essentially authority rather than replication as the source of truth in science.

I've heard from drug developers and many other people who tell me that they can't really make good decisions based on the scientific literature because they don't trust it. And in fact, drug

developers often conduct their own private replication exercises in order to see whether it's worth investing in the research, in the sort of follow-on from the research on which; if they can't trust the basic research before they make the investments, they have to replicate it themselves. But these private replication efforts efforts do not benefit the broader scientific community. What I intend to do as NIH Director is to restore replication and reproducibility of research as the core idea of what is seen as true in science.

In the past few years, we've seen so many episodes of of people, very prominent people, accused of essentially research fraud; people who lost positions, including inside the NIH itself, to these accusations. When you see so many people facing this exact situation of research fraud, the problem then is not actually one of moral failure by any individual scientist, but rather systemic failure that places rapid publication of results in prominent places and influence as the way to get ahead in science, rather than the establishment of true scientific facts, reliable, reproducible scientific facts, facts that are reproduced by other independent groups as the basis for advance in science. To change this, I intend to have replication become a core activity of the NIH and to reward scientists who participate in replication efforts.

So, for example, I intend to ask every institute to establish their own standards for what replication looks like in the fields that they cover, to fund researchers at an R-level who do replication work, and with the scientific community at large competing to ask: What are the key scientific claims in the literature that need replication? Claims on which people make decisions about drug development, people make decisions about their health, and people make decisions about what the next scientific steps ought to be. The practice of doing replication will become something that's normalized in the scientific community under my watch. Second, the problem with replication often is that there's no place to publish or gain scientific rewards for having done it. At the NIH, we're going to establish a journal where people who are NIH-funded and others can place their replication work.

It'll be a peer-reviewed journal with low gatekeeping so that the replication efforts can happen, but it's not. In the context of a scientific discussion about the reasons why a study doesn't replicate, what the next steps forward should be for research that does, and so on. There'll be a resource where the people who engage and work on replication can gain the kinds of scientific rewards that are now not available to them since top journals will not generally publish replication work. Third, and this is one of the most important reforms I want to implement, as far as replication goes, as things currently stand, researchers who are subject to replication, even the request for replication is a threat. Instead of the great honor it actually represents.

When a scientist has an idea and is approached by another researcher for replication, that should be seen as an honor rather than a threat. The scientist who is being approached for replication should receive rewards for that, just the kind of rewards that you gain from a citation, for instance, for a scientific paper. The scientists who cooperate with the replication efforts, share data transparently, and engage in good faith in these replications, again, should be rewarded. I'm going to stand up a new office within the Office of the Director of the NIH to measure these kinds of scientific productivities. We'll take advantage of other parts of the NIH

Office of the Director that focus on measurement of scientific productivity, but expand the scope to include participation and cooperation with research, with replication efforts, data sharing, and so on.

The idea would be that by measuring these sorts of pro-social activities, those pro-social activities were rewarded in the broader scientific community. We can turn around the current situation, which essentially has replication sidelined and viewed as a threat by people who have been replicated in something that's central and core to the scientific enterprise. And so that the scientists themselves will want to be replicated, will seek that replication because it will be the main way that the scientific careers advance. And the effect on fraud, well, it will undercut the incentives to commit fraud because there will be very little reward for having published a paper that isn't replicated. Next slide, please. Third, in work that I've done prior to the pandemic, I had analyzed the NIH portfolio of research, asking how new are the ideas that NIH-funded research actually supports?

In the 1980s, it turns out by measures of novelty of research ideas and research papers, it turns out that scientists in the 1980s, funded by NIH, tended to work on ideas that had been introduced only a year or two previously. They were the very cutting edge of research. With a few exceptions, in the 2010s, the NIH research-funded researchers were working on ideas that were somewhere on the order of seven to eight years old. At the same time, we've seen a graying of the scientific workforce with the age of first large grant moving from the mid-30s in the 1980s to somewhere in the mid-40s. Very slow progression for early-career scientists into independence despite many efforts by the NIH to reverse it.

The portfolio itself has tended to emphasize incremental advances that are very likely to succeed, rather than a portfolio where you may have failures for individual projects in the portfolio, but the portfolio as a whole is asking big questions so that you have the possibility of giant advances, cures for diseases that are previously seen as intractable, ideas for prevention, and other bold ideas. My goal will be to transform the NIH decision-making so that it has more of a bias toward bold and transformative ideas, not just for some of the mechanisms, but for nearly every mechanism that we do. We should be aiming for the fences. We should be aiming for huge advances. And the criteria of success then will be not that every single individual project can show some success in published papers.

That's not the key question. If a portfolio has every element of it succeed, that portfolio was not taking a substantial enough risk and swing for the fences enough to make big advances. What we want is the portfolio as a whole to succeed rather than just individual single projects. And so the goal will be to transform the NIH to thinking in this way. ARPA-H is supposed to do this, of course, but there's no reason why the NIH itself also shouldn't be doing this. Fourth. Next slide, please. Fourth item. The NIH has been at the center of the controversy over COVID origins. There are many researchers who believe that, and I recognize this is a controversial statement, but that many researchers believe that it's possible that COVID itself was the result of experimentation.

Of course, in the decade before the pandemic, there was a much controversy within the scientific community over the conduct of gain-of-function research of concern, where in 2014, President Obama had issued a pause on all such research. The regulation of this research is now the front and center of congressional action. And as NIH director, I wanted to work to make sure that the research we support does not pose any risk or harm at all to human populations. We should not be conducting research that has even any risk at all of causing a pandemic. And it should meet the highest ethical standards. At the very least, the public should have a say with the risks that researchers take. And so I'm going to make sure that I cooperate with congressional efforts and efforts by the administration to regulate the research that we do to meet the highest ethical standards and to make sure that it does not endanger human populations in the conduct of research itself. Final slide.

The NIH must foster a culture in which scientists can express disagreement respectfully, must encourage academic freedom. I've heard from people inside, intramural researchers inside the NIH, both during the pandemic and after, that they often don't feel this way. The culture of academic freedom in the scientific community at large during the pandemic, I can attest personally, was subject to substantial attack. The NIH absolutely must play a leading role in encouraging academic freedom. I've been working on a policy to guarantee, for instance, that intramural researchers in the NIH will have minimal oversight over whether their scientific research can be published, only subject to federal regulations or laws, but no substantive oversight so that researchers who find research results that, for instance, I don't like should have the absolute right.

To publish it without any say-so on my part. The kind of academic freedom that I thought we enjoyed as researchers before the pandemic is the kind of academic freedom that says you can find whatever results you like, you can have whatever discussion you like as a researcher, that is your absolute right to do so. Scientific progress depends on the right for researchers to dissent against scientific dogmas. And the NIH will work to make sure that we have, that intramural researchers have this kind of academic freedom and that we encourage the same kind of academic freedom in the extramural scientific community. Next slide, please. The last one, I think. Novel biomedical discoveries enhance our length and length of life are more vital to our country's future than ever. But that, of course, is the mission of the NIH. I'm going to end now and leave time, a few minutes for questions. Final slide. Next slide, please. Thank you so much, Jay. So we will now open the floor to council members for questions.

Okay, Monica, please go ahead. Jay, that was a great talk. And I wanted to say that I think you entered at a difficult time because of changes that occurred before you came between the election and when you entered. And I wanted to ask about your ability. I think you've been doing a great job in intramural and extramural trying to allay some of the anxieties that were caused by, for example, grant terminations, grants not going out, NOFOs, lots of things that were really different for the NIH than had happened before. I think you've been really trying your best. You've only been there since April 1st. to do what you can to allay some of those anxieties that people have.

I think that, like you said, science will change, but it was the rapid pace and also at times having adjudication of grants and terminations not by scientists created a lot of anxiety. My question is actually around the proposed NIH budget passback cuts in the passback budget. And that was sort of almost leaked, I think, last week. But it's more that your ability and your presence in Congress and your, have you You know, will you be able to be a part of those discussions with Congress when as the NIH director, when those come up with the ultimate budget of the NIH going in starting from June of this year, what's going to be proposed for the budget? Will you be able to be, as you said, in front of Congress like you just said?

Can't hear. Yeah, now we can. Jay, you're still on mute. Okay. Can you hear me now? Yes. Okay. Yeah, Monica, thank you for that. It has, as you say, it has been a challenging time. And a lot of changes have taken place, some for the better, some for the worse, for sure. I've been trying my absolute best to turn the light switches back on. So, for instance, the disruption in the scientific review panels, we have and I think by May we should be no longer behind. We've made it so the intramural researchers can order their supplies for their labs. We've turned on travel. I want science to continue in this country like it's supposed to, and I'm working very, very hard to undo some of the disruptions that have happened, I think in part because of misunderstandings.

And also anxiety over the political changes. A lot of it has to do with that, and I've been trying very, very hard to turn those back on. The business of science and biomedical science absolutely needs to continue. It's an absolute priority of mine to make that happen, Monica. As far as the budget passbacks, I can't comment specifically on the leak. Normally, this is a process that is a negotiation between the OMB and the agencies, including the NIH. I should say, just as a broad matter, I've spoken to many, many members of Congress in the context of my confirmation. And I've heard bipartisan support for the NIH continuing. And I've also heard, I've seen that President Trump wrote a letter to the incoming OSDP director, the new OSDP director, with his commitment that the United States lead the world in biomedicine in the 21st century.

And I will advocate to make sure that the NIH has the capacity and the resources to do that. Thank you. Thanks very much. Kevin, Dr. Johnson, go ahead. Yes, hello. Dr. Bhattacharya, very nice to meet you. I'm curious about, I love much of what you said in terms of some of the really disruptive approaches to kind of getting big ideas funded, generated, and supported, as well as the idea of a journal for helping with replication of studies. One thing that I didn't hear you talk much about is the training program. And I was wondering if you could just talk about your view of how the NIH should be involved in training people, especially given this potential focus on big ideas at a time when trainees getting their first grants probably won't come up with big ideas.

I can't hear very well. Your volume has gone down again. I don't know what I'm doing wrong, you guys. Sorry. Hopefully you can hear me now. Yes. Yes. Okay. I guess I just need to lean forward. Dr. Ernst, thank you for that question. It is absolutely vital that our training programs train the next generation of scientists and enable them to try their ideas out. I've done some research, again, before the pandemic, asking whether it was early career scientists or later career scientists who were more likely to try out ideas on the cutting edge in their own published

work. And the fact, slightly depressing for someone with gray hair like me, is that it's early career scientists who tend to work on the newer ideas, who work on the edge.

In fact, it's early career scientists working with mid-career scientists together that are the group that are most likely to try out new ideas. And so, for me, it is absolutely vital that we enable early career scientists to progress into independence as rapidly as they can, while still maintaining sort of the wisdom and oversight of later career scientists in collaboration. To do this, I've been thinking; I'm not sure exactly how to accomplish this, Dr. Nelson, but the kinds of ideas I had include, and I'm just at this point, I'm not sure this is, I think this is ready for prime time, but I'll just tell you what I've been thinking: Evaluating research projects on the advancement of postdocs in the independence.

Having 'Ks be instituted rather than having more institutional K awards rather than that individual so that when an early career investigator is hired by an institution, they can just have the researchers get the early career support immediately rather than having to go through a long K application, which sometimes takes years. Allowing researchers who have training support to but apply for our level funding rather than making that a restriction. I'm hoping to lots and lots of ideas on this. I think it's absolutely central for the future of biomedicine that we unleash the ideas of the early career scientists. I mean, I fully expect most of my ideas to be completely overturned by the time I'm done with my career. If not, then we haven't done a good enough job. Okay, great.

Rafael is next. Hi, thanks. Congratulations on your appointment, and thank you for your thoughtful remarks. My name is Rafael Rosario. I'm the chair of the Department of Data Science at Dana-Farber Cancer Institute. So I was particularly pleased to hear that reproducible research is a priority. That's an area I think deeply about, and it's one of the missions of my role as chair is to make that better in my institution. So I want to express my full support in helping advance that goal through my role in the council. I also was encouraged by your words on academic freedom, super important. So, I'm also encouraged to hear the continued commitment to the importance of funding, and I'm confident that this remains one of the most valuable investments we make as taxpayers.

So now, while increased support is an investment, of course, welcomed by scientists. I also want to express my confidence in the resilience and creativity of our current workforce to adapt and make meaningful use of available resources, even if they are reduced. So, with that all said, I want to share one concern. I hope you can help with and maybe you can share your thoughts on the topic. And it has to do with the current uncertainty. Monica made some remarks about that, around funding levels and areas of research that will no longer be supported and also institutional eligibility to these funds. So this uncertainty makes it difficult to plan strategically whether it's hiring or collaborations or long-term research commitments. So any clearer guidance we can get from the NIH I think would be very helpful.

So thank you again for your leadership and for taking the time to engage with Council. I look forward. To supporting your efforts however I can and to hearing your answers to these

questions. Thank you. Rafael, thank you for that. I mean, I, as I said, have come from academics myself, so I understand entirely what you mean about the uncertainty. This is the main reason I want to start pushing as hard as I can to restore regular order. Even if we are changing and shifting some research emphases toward this Make America Healthy, as long as you can plan around it, you can devote your time and efforts to it. So, I mean, I think there's been, I think, two classes of disruptions. One, I think, healthy and one less healthy.

One is the emphasis on making America healthy and a shift away from, I think, sort of more politicized scientific ideas toward research that is directly aimed at the health needs of the American people. I think that's a healthy thing. That's automatically going to cause some disruptions because the kinds of research projects that sort of, for instance, fall afoul of the president's executive orders, you're going to have less of that. But at the same time, the commitment to make sure that every single American, no matter what their race, sex, you know, their sexual orientation or whatnot, that their health needs are reflected in the portfolio of the NIH, I remain entirely committed to that. And so I think that is going to be ultimately a healthy transition, so that we, the researchers of this country that receive support for the NIH, are focused on the actual health needs of the American people rather than fighting political battles that we're ill-equipped to fight.

Sort of less healthy part of it has been disruptions, I think, caused by the fact that, I mean, just to be very blunt, there's a lot of distrust, mutual distrust between folks who voted for President Trump and generally the scientific community. The scientific community, I looked at some of the the Pew estimates of the public confidence in the scientific community to act in the best interest of the public. And they're shockingly low. I think it's like less than one in four Americans actually believe that scientists work for the benefit of the American people. And on the other side, of course, scientists have deep distrust of this administration, for better or worse. I think that a lot of the disruptions have happened because of that distrust, again, on both sides.

I don't know if I can accomplish this, but when my goal is to try to build a bridge because I don't see in President Trump or in the folks I've interacted with any desire to remove support, public support for the biomedical enterprise. In fact, quite the opposite. Basically, universally, I think, if the biomedical enterprise is working for the advancement of the health of the American people, we're going to get universal support for it. At the same time, scientists need to understand that what happened, especially during the pandemic, has really driven a wedge between scientists and the American public. sort of talked in ways that are more respectful for the concerns the American public has; talk and work in ways that are respectful of the way the American public has.

I don't know, again, if I can succeed, but that's my goal, is to build that bridge. I mean, I do think that science can't work without the support of the American public. American science can't work without the support of the American public. And American scientists in exchange for the tremendous support that we do get from the American public, owe it to the American public to develop increasing life expectancy, answers to the chronic disease problems they face, and avoid the sort of politicization of science that I think has led to this moment. Thank you. Great. I

recognize that we are at time for this session, but this is obviously a really critical dialogue. And so if Jay can continue for a few minutes, we are more than happy to continue to extend this session.

So I'll turn it over to Kent, who's next. Hi, Dr. Bhattacharya. Thanks so much for coming. And I think we all share your love for the NIH and want it to remain a crown jewel in the federal government. And I think you'll find us all on the council wanting to do everything we can to support your efforts to ensure that happens. Very briefly, I think I'm the only veterinarian on the council, and so I wanted to ask you about animal research. As you know, DCAPIPSI supports a lot of animal research in the biomedical research field, including training those who are using animals and veterinarians using animals for research and veterinary training. Could you comment on your perspective on support for annual research? Do you foresee any changes coming up?

Is the reorganization that may be happening in NIH might impact that? Any comments you might have, because it is a very important subject. Thank you. Thank you, Ken. So, this is an area where I'm still learning. So, I'll just start with that. As a general matter, I think that animal research should be reserved when there's almost no, where there really isn't an alternative. And my understanding is that in recent years, they have become available, alternatives in many cases. I don't think we should be dogmatic about it, but I do think that we should be having an understanding about the ethical concerns that many do have about animal research. And again, just reserve it for when there really isn't an alternative. For this, actually, maybe I can ask Nicole to weigh in.

Nicole's been working on this area quite extensively for years, and she's going to be a close advisor to me on this. Absolutely. Happy to win. Thank you. So as you indicated, you know, animal research has for decades supported advances in biomedical research. But I think we have insights from the drug discovery space and from the environmental toxicology and health space. That demonstrate to us that we can leverage advances in scientific discovery to actually do better and to move towards more human biology-based methods, whether that's computational models, complex in vitro systems, likely integration of all of those different types of technologies. And you probably remember, and others may, that my first interaction with Council of Councils actually was to discuss the concept of the complement animal research and experimentation; the complementary common fund program which is now, you know, a full-fledged program and is in the process of reviewing applications and making awards soon for really exciting new technology development centers.

And part of this program will be a validation and qualification network to develop validation data packages to help ensure that those new approach methods are really robust and reliable, and replicable; then can be translated into better public health protection and additional human biology-based insights in the biomedical research arena. Many of you may have also seen the press release and the scientific roadmap that the FDA put out two weeks ago, where they really highlighted their intention to put much more support and resources towards supporting this transition towards bigger and better reliance on new approach methods for preclinical safety

testing, beginning with monoclonal antibodies. But they also alluded to kind of a generalization across the preclinical safety space to help enable better drug discovery and human-relevant safety assessments.

And they called out NIH as a partner, a really critical partner; they also called out the interagency coordinating committee for validation. Of alternative which as you know is a committee mandated by Congress that spans across 18 different federal partners across the government. And so I think there's a lot of momentum in this space and there's going to certainly be I think a renewed focus and energy put into ensuring that we are using the best science possible to support biomedical research. Mechanistic insights and discoveries and public health protection. Thanks. I'm encouraged to hear that you mentioned the need for validation of the NAMs. Very, very important before transitioning into human use. So, wonderful. Thanks very much both. Thank you, Ronda, please go ahead. Thank you so much. I really appreciate the vision that you've brought forward.

And I can say, I almost want to say hallelujah to some degree. From the standpoint of you, many of the things that you mentioned have been long-term things that I've observed, but also wondered whether or not there would ever be a change. The first thing is reproducibility. I've been with the NIH in advisory capacity now for 12 years. And the whole issue of reproducibility has always been a thorn in the side, primarily because I was always told it was not funded by NIH. The problem with that is that the adoption of research that shows really good promise is hard to make that translation into the arena of the real world, accepting that particular research. So I really, really

um support what you're saying, I would also add that maybe as part of this reproducibility, that the the next study also be done in the real-world setting with large numbers; it's one of the things that many times it's absent, particularly if it's relegated to an academic setting that doesn't have the reach as some of the other players in the field like health systems, insurance companies, employers-all of them have larger reach. Many of them have the data that you're talking about, and certainly can and have been engaged in reproducing research on their own. So I just want to bring that up. Um, to say also your your emphasis on data data transparency and I'm hoping with that some standardization so that those that are engaged in research are using some standard parameters that will allow there to be cross-comparability across many of the populations and many of the studies that are out there.

I particularly want to mention all of us as being a very good example of being able to use their ability to recruit the public, but also beginning to recruit other partners in this type of venture where you're collecting a wide range of information, allowing researchers to go in and begin to create novel ideas and findings, which is very, very exciting. And I think that is one of the things that is very, very important and certainly has been done. The last piece I have is around communication. I think one of the things that is certainly has been not without a lot of effort on many parts of NIH as well as National Academy of Medicine and others have been in those circles. It seems as though we're not able to communicate effectively with the public to help them understand.

And I think you're absolutely right that this trust that grew tremendously during the COVID era had a lot to do with not understanding, not even realizing that science is iterative. Particularly when it's something new, you don't have the absolute answers at that point, but the public wasn't listening or hearing or understanding that. So, I'm hoping that part of your initiative will devote time, effort, and resources to being able to communicate on a layman's level to help build their literacy as it relates to what is being done so there's more acceptance of the findings that come with time. So again, thank you so much. For your ideas, because I think they're definitely well-needed, and I certainly see this as being exceptional.

I work with UnitedHealth Group, and the things that you're talking about are definitely the things that are very, very important from my standpoint of view in our organization. Thank you. Rhonda, thank you for those comments. I mean, I don't have much data. Let's work together on these things. Availability of data resources at scale, researchers more easily, reproducibility standards, Stanford's reproducibility for the different disciplines and institutes, all those are quite important to me. I think as far as the last comment about public trust, one idea that I had was that before I became NIH director, I was running a podcast with the name Illusion of Consensus, and then another one, Science from the Fringe. I'd like to use some of those skills that I gained interviewing scientists.

The aim of those podcasts was the public at large, to bring scientific ideas that people maybe hadn't seen to the attention of the public in a way that's understandable to the public. I think our science communication efforts at the NIH, it's sometimes difficult for me on the outside to tell who they're aimed at. Are they aimed at other scientists? Are they aimed at the public? If they're aimed at the public, it was often, I always viewed it as, you know, like the people, we were talking down to regular people rather than trying to talk with them. So I want to work to fix that. I mean, I think our communication with scientists is actually pretty good. And we have PubMed, for instance. We communicate with scientists all the time in languages that scientists benefit from and understand.

We can do better, for sure. But our communication with the public, I think, needs improvement. And I'm going to work hard on that. One thing I would suggest, think about what the public goes to. I know it may sound like a dirty word, but social media is so strong and certainly an avenue that they go to. They just don't have something that gives them a seal of approval that this is legit and that this makes sense. So I'm just going to say that and leave that alone. I think we have no choice. We have to deal with the public where they are. I actually like social media. Uh, found Twitter to be a very effective way to reach the public.

Um, before I became an Ice Director, uh, we need to update our our strategy so that um, that we reach the public where they are, in the language they understand, and not talk down to them but actually have conversations with them. I think that's the way you build trust, okay, great. Gene, thank you so much for sharing your vision with us. We really appreciate it. And there's so many things that we aligned on. One of the things that I need clarification on, if you could help me understand, you talked about academic freedom and supporting academic freedom. On the

other side, I'm thinking there are topics that we're not ready to fund at NIH anymore, if I understand this correctly.

So I want clarification on, for me, academic freedom is you know, the ability to study whatever it is I want to study and how does that fit together? And the second thing is more in alignment with what we just heard. I wondered if there was a way that we could approach what I call science and society. That is a dialogue. between the general public and us. We talk to each other all the time. We get it. We get each other. We understand it. We're in the same ecosystem together. But I think what we're not doing well, and I totally agree, is reaching the public where they are. But it's still, again, to me, that communication can't be one way. We can't talk at them, as you said.

When we speak with them, I think we have to bring them into conversation. So I'd love to see us stand up an office that's rather robust in having those conversations because we can't build trust without conversations. We can't tell them what we're doing and they can't say, 'I hate you for this' or 'I don't trust you.' It's not going to work in the long term. So for a sustainable model where science and society interact in ways that you just talked about in a podcast or many of those, it can't just be one route for us to understand this. But I'm really struggling with: I think we work so hard on behalf of the public and yet they don't know it.

So that's that's a struggle, right? That's a real struggle. That's a sadness, actually. So how do we try to address it together? Thank you for those questions. So first on academic freedom, I'd say I think to me, the question of academic freedom isn't can I work on anything I want? I mean, that is part of academic freedom, but But it's distinct from what the NIH has limited resources. So what does the NIH invest in? To me, the key question is, are we investing in things that will meet our mission, advancing the health and longevity of the American people, advancing science to advance the health and longevity of the American people? That's the question. So that's not a question of academic freedom.

That's a question of how do we uh shepherd scarce resources so that we meet the mission but within that there should be academic freedom, right? So the if I if somebody uh writes a paper that has a scientific advance that contradicts an idea that I've had, even though I'm an NIH director, that person should have the absolute right to be able to publish that paper and to say what they believe. They should be able to contradict me or anybody else. Science advances when people disagree with each other, have different concrete hypotheses, and then you do experiments that determine one is right and one is wrong. And that discussion really is the core and heart of academic freedom.

As NIH director, of course, I don't have any capacity or any desire to stop people from saying and thinking things that they want to say in the scientific community at large. The power that I will have, and of course it's limited and advised by you all and other folks, is where do we put our scarce resources so that we advance the health of the American people? I think there's a subtext, I think, to your question, Gina, I want to address. The President's order on DEI initiatives, I think, are one of these things where I think it's misunderstood. I don't think that the

DEI initiatives, I read those carefully, and I don't think that they're aimed at stopping fundamental research that advances the health and well-being of minority populations.

I wouldn't have accepted this job if that was the case. I think that the health and well-being of minority populations, as well as every American, are a central focus of the NIH and will continue to be under my watch. And so the question about DEI, in my view, is more of a political ideology. And just from the point of view as NIH, as shepherd of the NIH funds, I think that money put to that will have less of an impact on the health and well-being of Americans, including minorities, than money put to directly addressing chronic disease prevention. How can we prevent chronic disease, which afflicts minority Americans at higher levels than many others? So that, I think, is the maybe – I hope I addressed your first question directly.

As far as the second question, you know, the means of communication between the public and scientists – I mean, I think it's just hard because we're so used to talking to the public in a certain way. I remember when I was a young scientist, the first time somebody approached me asking me if I'd work on a press release, I thought to myself, why is this my job? I shouldn't have to do any of this. What I found, though, in the last few years is that interacting directly with the public really does help. It sharpened my scientific ideas. It helped me see where I fell short as a scientist in communicating. And I think it's, although sometimes bruising because, you know, you hear things you don't want to hear, it's really vital.

And I don't know. I'm going to try to lead by example on this and work on it. And, Jean, any questions? Any suggestions you have or if we can, if you're working together on this, I'd really welcome. And this is one of these things that's going to be hard, but really essential if we're going to regain the trust of the American people. I'm really happy to work on this. I think about it all the time. And the first thing you said about DEI, thank you for saying that. I still think there's probably massive misunderstanding about exactly what it means and it doesn't mean. Well, Jean, to the extent that it things that advance the health and well-being of people, the NIH will support it. That's my litmus line. Thank you. Okay, we are going to take two more questions and then I'm going to cut this discussion to a close, unfortunately, although I'm sure we could all go all day. But I want to be respectful of Dr. Bhattacharya's time and of the very full agenda that we have for the rest of the afternoon. So, Monica and then Linda, please. Thank you.

I think it is tremendously reassuring to hear your perspective as a longstanding scientist and someone who cares about the health of the American people. As an infectious disease researcher, it's hard for me not to bring up global health research. And the reason is that HIV is a chronic disease. Certainly in no way does the entire budget of the NIH go towards acute diseases. I think it is generally skewed towards chronic diseases, including the chronic diseases in infectious disease, which are hepatitis B and HIV most prominently with after effects from tuberculosis. So did want to bring up your ideas on global health research and the translation of that work that's done in prominent places like South Africa, which absolutely has the highest HIV burden, to the health of Americans.

Most of the work that has led to treatment paradigms, prevention paradigms, how to screen for resistance has been done in global settings. Absolutely, the benefits Americans because that's how I know how to treat HIV is because of a big study done in South Africa. So I wanted to ask about, and certainly that applies to air pollution, to clashes, to violence, to so many other things that may be more high-prevalence in a specific region, but benefit Americans. So that was my question. So, thank you, Monique, for that. So, I think the portfolio of the NIH has a long-standing record of success in collaborating in research in other countries. I mean, and I think it should continue to have that.

That said, it's incumbent on us to make sure that that portfolio really does translate and benefit the health and well-being of the American people, which is, of course, the mission. And I think specifically for HIV, you know, with there's been recent advances, which I think open up, like, for instance, Lencapavir, I think, is the drug that actually, I think you take it for, and you can prevent HIV for up to a year almost, I think. So absolutely remarkable product. And that opens up new areas of potentially even thinking about how do we eradicate HIV from this country? I mean, and I think, so looking at the portfolio of HIV investments, I think, I mean, we always want to make sure that we are using our dollars for the most important things, right?

And I'm aware, as you've told me many times, Monica, about the importance of the trial networks in South Africa, for instance. Yeah, sorry. No, I mean, I appreciate your advice on that on all fronts. But I do think that looking carefully at this portfolio is something I intend to do. I don't want to make any rash decisions, but the key touchstone will be: Let's make investments that advance the health of the American people. And I anticipate that there will be some changes, but I don't know that we— I don't, I'm not— I don't have any intention to stop working in foreign countries. That would make, I think, would actually harm the health and well-being of the American people. So we can work together and go forward. Thank you. Yeah, I'm Linda Chang.

I just have a very thank you, first of all, for that wonderful overview of your vision of NIH. And I really agree with all of your points. I just didn't hear a discussion about whether you have plans on the, we've been hearing about the NIH institutes are going to be reorganized and whether you have any specific plans already for that. I'm just curious about that; this is a quick question. Well, thank you Linda, thank you for your comment. Um, I-I don't have any specific plans for reorganization at the moment. I know, I know, I've talked with members of Congress who have plans. Um, I think the OMB had a plan, um, and um, I've read also all of the documents going back now decades on reorganization ideas for the NIH.

I'm going to work with the administration and with Congress on this. I'm not planning to go rogue on it myself. I think any reorganization is going to have to think through carefully what will be gained from it. If it's just reorganization for its own sake, it won't make any sense. But if it really does result in collaborations that would not have occurred, you know, reductions in duplication of efforts that don't actually advance the idea of replication very much, things like that, then it might make sense to do it. But I'm going to rely very heavily on advice. There's an SMRB

process that Congress actually put in place for this exact process. So I'm thinking about maybe using that if there really is a lot of desire in Congress to do this reorganization.

I'm not planning on doing anything half-baked on this. So you don't see this happening in the very near future? Because there were rumors that they were going to decrease the number of institutes down to eight institutes or something like that. That just sounds so drastic. I think there was a leak of the OMB memo. Yeah. But again, Linda, that was the beginning of a negotiation. I don't know. I mean, we'll see what the end point is. It's hard to forecast exactly. I personally have no plans to do anything without lots of advice, okay, thank you, okay, great, um, thank you all for such a robust discussion, and thank you so much, um, Jay, for your remarks, um, both your presentation and your thoughtful consideration of the questions posed to you by council members, and for spending some extra time with us; I know you have a very busy schedule, so thank you for that.

Okay, we are now going to move on to the next presentation, which is from Marina Volkov on the Council of Councils Working Group on Science of Science. She is the director of Deepa Gipsy's Office of Evaluation, Performance, and Reporting. So, NIH has a long history of engaging with researchers to generate evidence to inform improvements to its programs, policies, and processes; The Science of Science, which is also known as meta-science, is absolutely crucial for understanding these processes that shape scientific discovery and innovation. So by analyzing patterns and funding collaboration, publication, and reproducibility, this field can really help optimize research practices and improve resource allocation, particularly in a constrained environment, and enhance our scientific impact overall. Ultimately, this work really strengthens the credibility and reliability of scientific knowledge, and applying scientific principles to help us understand how to better support and shape science is really a crucial role for DeepAkypsy.

So we recently solicited applications for a pilot Science of Science Scholars program that will bring experts in the science of science to NIH to work closely with staff to help answer critically important questions to improve NIH processes, policies, and programs. But there is more that we can do. We think this deserves further broad consideration. So, that's built into a proposal we have and that I would appreciate your feedback on. So Marina, I'll turn it over to you now. Nicole, thank you very much. I appreciate that introduction. It's actually that was great coverage, and I'm going to see if I can make up some significant time for you all because Nicole really laid out what it is that I'm here to discuss so I can skip through.

As Nicole mentioned, there is this very robust interdisciplinary field of the science of science, or meta-science, also where people truly are studying the scientific process itself and what I'm here to talk about today is how can we work bring that kind of robust scientific inquiry better into NIH to allow us to answer many of the questions, or to begin to answer many of the questions that have been discussed throughout the day today. I feel as the whole conversation that we had this morning with Dr. Bhattacharya just now really begs the question of how can NIH better understand how the things that we do are meeting our mission and how can we improve upon that? So that's really the crux of what we're talking about. Next slide, please.

And again, I'm not going to go through this because I think this is really what we've been discussing throughout much of the day. Next slide. I want to point out that this is a question NIH has been grappling with for some time. Back in 2014, the Scientific Management Review Board, the SMRB, published a report in which it recommended that NIH have a systematic and comprehensive approach towards studying itself. And we have been working steadily on this systematic and comprehensive report approach. And if I can go to the next slide, please. There are many external folks who have been saying the same thing. thing that is is of great importance so in this science of

science field by bringing the external people in to help us better answer these questions one disconnect that has always existed between the people in the external world studying us and those of us working within is there's always been a bit of a disconnect in terms of the questions that are of interest to those people external to us versus those of us internal. And the questions of interest, as well as for those studying us externally, NIH is a very Byzantine place, and we have very complicated data, and we have data that we do not make it available to everyone because it is also proprietary data. Earlier today, when talking about HRHR, the question came up of looking at those unfunded applications.

That is just one example of proprietary data that we cannot share outside of the NIH firewall which has always been a frustration to the people who actually study us and actually, if we can go to the next slide I'm going to skip over going some over some of these factors so again Many, many researchers have been studying us from outside of NIH. I want to point out in the middle of this, this is just a handful of examples of important studies. You'll see Dr. Bhattacharya, he referenced this study that he published. Published on Does NIH Fund Edge Science? So he has been working in the science of science area. I also want to point out to the left, the 'Race, Ethnicity, and NIH Research Awards' is a paper that came out in 2011 by Donna Ginther and colleagues.

And I just want to mention this paper in particular because folks have been referring to this for years and years at NIH as the Ginther effect. It had real impact in how NIH approached support of the research community, and we need more work such as the Ginther paper to really help us understand what we're doing, how we can do it better. So with that, next slide. So this scientific field, the science of science field, is primarily funded through for public funds through the National Science Foundation. Back in 2006, they began a program known as the Science of Science and Innovation Policy, SISIP. The name has changed, but the point of the program remains the same. What evidence can be generated by the scientific field that can help policymakers in improving upon what we do?

So this whole idea of this program was to really create an evidence base for policymakers in making decisions on how best to conduct scientific research, so back and next slide please. In 2019, our National Institute of General Medical Sciences partnered with this program to create a subset of the program and to really support those studies that could examine important aspects of the biomedical research enterprise. So Science of Science Bio has existed since 2019. It's an

interesting program because it is truly conducted in partnership with NSF and the review, the management of the review aspects, the receipt of grants, all of that is handled by NSF. Then the funding of the grants is done by NIGMS and the management of the grants moving forward I wanted to give you just a handful of examples with the next slide please again these are just a few examples of things study that are being studied within that and you can see that they these grants can look or these grants

Projects will look at the impact of NIH policies on the conduct of science. There are grants to look at the support for resources and methodology development and what is the benefit, what is the impact of those programs. There are studies to look at the workforce and how we support the workforce, what is the best way of going about. Maintaining the pipeline of researchers and there are studies on data sharing and the impact of data sharing and what it means for science this is just examples of the type of projects that are funded within this, in addition to this grant program. If we can go to the next slide please, we have many different ways in which we have been engaging with the science of science research community.

We've had several meetings, this is just listing a handful of them, where we tried to bring together again, the NIH policymakers, the NIH program folks to work closely with this research community to help create that handshake where the questions of interest align to identify those. And along those lines, we participated last year in something with OMB. OMB, and I didn't go into it there, the Evidence Act, the Foundations of Evidence-Based Policymaking Act, known as the Evidence Act, was passed in 2018. As part of the implementation of that act, OMB is trying to create opportunities for handshakes between federal departments and the research community. And we participated in that where we were able to publish on the OMB portal what are the questions of greatest interest to NIH that we would hope that those external to us would study about us.

And that generated a lot of interest, a lot of interesting conversations, and hopefully, at some point, a lot of very interesting research results. That NIH can then implement. And then Nicole mentioned our Science of Science Scholars program. Right now we are working on a pilot of that, and where this is done in collaboration with our Office of Extramural Research, where we plan to bring in Science of Science Scholars. There's no money involved. They will be special volunteers, but they will be working very closely, not only will they have access behind the firewall to all of NIH's proprietary data, but they will be working very closely with those people who understand this data the best. As I mentioned, the data can be rather Byzantine at times and getting through that, but by working together in partnership, we're really hoping that this is a unique opportunity for us to learn from the field some of the methodology that they would apply towards examining that data and for

those working in the field to actually get their hands on much of the data that they are hoping to get on. And there are many other examples that we can talk about how we're trying to engage with the science of science researchers. NEXT SLIDE, PLEASE. AND I'M TALKING REALLY FAST BECAUSE I AM TRYING TO GET US CAUGHT UP A LITTLE BIT ON TIME AS MUCH AS POSSIBLE. I WANTED TO END WITH WHAT I THINK IS A REALLY FASCINATING

EXAMPLE. We have been talking throughout the day about Matrix, and our folks at the National Eye Institute in collaboration with several other institute centers and offices have launched a challenge to try and create an index that could really measure to some degree exemplary data sharing as examples, or how effective is a researcher in sharing their data?

Is there a way that we can begin to capture the effectiveness of data sharing? So I thought, as I said, just wanted to end with what I thought was an interesting example. And then if we go to the next slide, you'll see, so what is next? Where are we going to go? How do we begin to realize the recommendation of a systematic and comprehensive way by which NIH can continually strengthen its ability to study itself, and how do we engage with the external science of science community to help us do just that? And we believe that these questions and more could be answered by a Council of Councils working group. I want to point out that we're not

looking for the working group to come up with all the new metrics and indexes and etc that we need but rather to help us to really think through best ways of engaging with with the field but also to think through best ways for us to approach it how can we be more systematic and comprehensive in our approach towards studying ourselves And with that, I'm going to open it up for questions, comments, and I apologize if I went really fast, but as I said, I think we talked an awful lot earlier today about some of these ideas. Thanks Marina, I really appreciate your dedication to getting us back on time as well So, if council members have any questions or comments, please raise your hand and I will call on you and ask you to unmute yourself Kevin, please go ahead Hi, thanks a lot And Marina, nice to meet you also I'm Kevin Johnson from Penn.

I'm curious, you know, there was a time when council and the NIH were thinking about science communication as a more organized activity, especially the teaching of science communication. Do you see any synergies between that idea, recognizing you may not have ever seen that concept, and what we're trying to do with the science of science? Thank you for that question. And I'll admit, I've been around NIH for quite some time, and I knew we actually had a grant program on science communication at one point. And I actually, I think that science communication, so much of what even Dr. Bhattacharya and you all were speaking about beforehand, the public, when they ask NIH, 'What are we getting for our investment in NIH?' We need to be able to tell them something other than, 'Hey, we had a lot of really good publications in science.' And how can we, by better assessing and evaluating ourselves, how do we generate evidence that will also tell the public this is what you're getting?

And it's a very, very tricky story to tell because NIH produces the evidence base that others then use to improve health. And how do we tell people how this happens? How do we tell people about how science is implemented? How do we know when NIH research is directly led to something that directly benefits the public? So, I think that science communication, how to communicate with the public better, is of vital importance to this effort. Thank you. Thanks. Jean, please go ahead. Sorry, Rhonda. Sorry. My fault. Please go ahead. No problem. No problem. So thank you so much. So, I have a couple of questions on this, primarily from the standpoint of

yours. I'm wondering whether or not there is a sector of science that may not necessarily be part of what one would typically focus on.

And let me clarify. I kind of hinted that in several of my questions today. AND THIS PARTICULARLY IS IMPORTANT IN TERMS OF LINKING SCIENCE TO APPLICATION IN THE REAL WORLD IN THE DELIVERY SYSTEM. Certainly, we don't want to keep the 17 years it takes from a scientific fact to actually being adopted in practice. And so we need to escalate and move that quicker. So one of the things I would wonder is whether or not in the science of science, would there be areas where you would look at what the outside world needs from the standpoint of view of care delivery? Because there are many gaps out there that, and I'll say my colleagues are not very good at communicating those, and probably need to do that, but to help the research area to understand where the pain points are, but also you as the research area connect with those areas that create

guidelines, consensus documents, and the new term now is playbooks that actually demonstrate how to operationalize some new science in some way to help bring the reliability of implementing it with effectiveness. So my thing is there's another area that needs to be thought of. Number two, we need to go beyond what NIH can do. NIH has to, needs to join hands with the consensus organizations, as well as the funding organizations that kind of fund non-research-based new infrastructures and functions within the healthcare delivery system. I hope that wasn't too confusing. Oh, no, no, no. And I want to tell you that I agree and have resonated throughout the day with the points that you continually make. Again, NIH only can achieve its mission if others take the research that NIH produces and actually apply it.

And to understand that handoff, to understand the chain of evidence, the evidence flow that goes from research into practice ultimately into improvements in health and then the spillover effects, that's the number one question I think that this this effort has to really start to look at different ways of building that chain of evidence and understanding and finding the markers of when it actually does happen. I will say one thing we have talked extensively with even within our own department in order for NIH research to have any impact it needs to touch other parts of our own department, whether it be FDA or CMS, etc how do we begin to know, how do we begin to capture that evidence flow of NIH with other parts of its sister organizations within the department, not even going to the outside, to the practitioners, but even to begin by understanding evidence flow within the department.

If you look at the SMRB report on the value of biomedical research, it's all about how to make that how we can strengthen our ability to capture that chain of evidence as it flows from research into actual changes in health. I hope that addresses [it does]. And I hope that part of the scope of work that out and create those relationships that allows that to happen. And certainly, we'll be very interested in that. I'm going off council, but very interested in that being furthered along. Well, I hope that we can continue to ask for your input on these things even. Okay, great. And Jean, please go ahead. Thanks for bringing back the Ginter effect. I have to say I still think about it, and I was so grateful for that study.

We all had stories to tell, and finally she sort of brought the data together to say that there was data to support what we thought was happening anyway. So I agree. I still talk about that study. It's over a decade old, I think, by now. But what I wanted to bring to this is as we talk about communication, I think the general public understands stories. They understand narratives. They may not understand a particular channel and how I could block that channel or whatever it is I could do, but they understand if a drug worked for a certain person in a clinical trial. We have to put more of those out there, those stories from people in their communities, in their neighborhood who just said, look, I was on this clinical trial.

This drug helps my son. It helps me. I think we want to bring personalized stories to this. I think when scientists do it, we're talking about the inclusive data of everything we studied, the graphs, the statistics. We may lose them. I don't say we always do, but we can. But I think a story doesn't lose someone. And I think we have to be better at telling stories. And I agree, some scientists are not good at it. That's not what they want to do. They're introverts. They want to be in their labs. I don't think they are the ones that we necessarily need to be explaining their science. We have to have people who communicate science to others in society in a way that makes sense. It doesn't have to be the researcher themselves.

It can be if that's their proclivity and they're good at it. It doesn't have to be. I think sometimes we miss the point by having a scientist try to explain it in language that they're not used to using and they're not comfortable with. I think we need to find ways to actually have interpreters of science who could talk to the society and people at whatever level they're at, to make sure that the stories get through to them. But I think if somebody said, 'I was cured of this illness,' or 'this thing happened to me,' or 'my son is better because of this, he was on the autism spectrum, this is what happened,' we have to communicate stories if we want to reach everyone. Everyone gets a story. Agreed.

And we need to be able to capture those stories and to really have on hand those stories to supplement whatever other kinds of approaches that we have towards understanding our impact. So, relatedly, we also, you know, we won't be able to study everything that NIH does, so we also relate to being able to tell the story is to be able to study actual case studies. Can we find good examples where science has worked the way that we want it to work and has resulted in ways that we have captured in changing health, in meeting NIH's mission? Can we find those stories and package them in a way that the public can understand? We have many of those stories, so yes. Yes, we do.

And our office, that is one of the things that our office works on as well. Okay, great. Susan, please go ahead. Yes, thank you, Marina, for your comments. But one thing that we haven't mentioned is that basic research sometimes is basic research, and is not really rediscovered for 15 or 20 years. NIH keeps changing. Some thoughts are You know, funded today, but not funded tomorrow. How can we be sure that we really first support basic science for the sake of investigating something that is important, that maybe later on is going to be used for human health and to improve the health of Americans? But how can we make sure that we capture those stories and we link them all the way through the years to current discoveries.

Yes, and believe me, we have been talking about that because in the instance of basic science too, how do we begin to show how a discovery here had such influence in so many different ways? How do we show the diffusion of that finding? For example, CRISPR has been used many times to show just that. This is what CRISPR has meant in so many different areas. How do we begin to build more examples such as that? And once we have those examples, what do we learn from them? How did these basic science discoveries, what was it about them that made them diffuse at a certain rate, or what about them can we repeat in further support of basic science? Thank you very much. It's just sometimes there's findings of serendipitous that are interesting.

They're so basic that maybe we don't even know how they're going to be applied. They're just super fun and interesting, and they need to be published. Yeah, we used to talk about, is there a way like you can tag a bird and watch the bird's migration? Can you tag an idea and watch it migrate throughout science? We have talked about that quite a bit. How do you know in 20 years when this one finding has resulted in many different impacts? Thank you. I would also add, from my perspective, while this is incredibly important to highlight success stories, I think that part of the science of science is also taking a critical and transparent look at where research has not succeeded and understanding, you know, where there are also sort of negative findings or lack of translation and, you know, really putting a transparent lens on that so that we can learn from our I don't want to say failures, but our negative insights just as much as our positive insights. So that's just one thing I would add to this discussion. Kent, and then I think we'll move on. Thanks. Yeah, I just wanted to say I think it's a great idea. I fully support if we're going to vote on this to proceed with a working group. Thanks.

Okay. Wonderful. Thank you all for your comments and your ideas. I don't think that this is a decisional agenda item, so there will not be a vote on it, but I think it's clear that there is support for having a working group on the Science of Science. So, thank you all for your feedback on that. So our next concept clearance is from the Office of Strategic Coordination. So this new concept is entitled the Cellular Senescence Network, or the SenNet program. It will be presented by the NIA director, Dr. Richard Hodes. The presentation will be followed by comments from two assigned council member discussants, Drs. Kent Lloyd and Dr. Jennifer Manley. Richard, I'll turn it over to you. Thank you. Thank you very much for the opportunity to present.

Just to clarify, if we turn to the next slide, this is not a new initiative. This is a report back to you on the results of the first phase, which was approved and monitored by the council. And now I have the opportunity to present to you a proposal for moving on to its second stage. This is an outline of the concept. What I'll go through in some further detail is the productivity of the initial initiative. The process that's gone into the formulation of the proposal for the second stage and then the information which may feed into the informational vote for approval again of the extension to Phase Two of the Seller's In Essence Network or Send Net Program. Next slide, please. So thanks for all who have been working over the past nearly five years on this.

Dina Singer, a partner from NCI with NIA, UA, and Chimeli have been enormously effective as program coordinators, and Tanya as a Common Fund program leader, and all those you can see here representing input from multiple of the institutes at NIH because, indeed, Sellers In Essence turns out to be something of importance to the basic and translational missions of nearly every one of the NIH institutes. Next, please. Just a background on cell senescence. Many of you are very aware that the concept really only appeared as a reality in the 1960s when it was first noted that cells, normal cells, non-malignant cells, even in tissue culture, had a finite replicative capacity after which they stopped dividing and sat there. They don't just sit there, though. They have characteristics which are an important part of their biology.

They have normal biological roles and are important for things such as wound healing and embryonic development. They also play a role as they accumulate in nearly all species examined with age and contribute to aging conditions and diseases. They're very rare, so their numbers are small, even though their implications and consequences are great. And the mechanisms that are responsible for senescence going into this initiative in particular are not very well understood at all. Hence, the Common Fund launched the Cellular Senescence Network nearly five years ago to study senescent cells and their role in healthy aging and disease. Next slide, please. So a bit of the impact first. I'll go through the specific components of the program, but the productivities include the generation of some 1,300 data sets, over 780 of them now published, many of the other protocols for study of senescence published.

To the right, you see a summary of the tissues of origin and the kinds of multiple omic assays that have been carried out to characterize these cells. Next slide, please. This is a network visualization of the way in which some 15 human organs and tissues studied with 327 different biomarkers sort out and send that as it's been defined over these past years. Next, please. In addition to identifying the senescent cells and their heterogeneity, the process of doing so required development of novel tools and technologies, some of which are listed here. So, for example, a radio tracer that visualizes beta-galactosidase. That was one of the earlier markers noticed in cells that were senescent. Here, though, amenable now to PET and MRI imaging, as well as several, as you will see, bioinformatics, tissues transcriptomics, and spatial transcriptomic techniques.

What I'll say is remarkable over these past five years is that the techniques to develop this initiative to the stage it's at actually were largely the result of the early phases. And when we go still further, the use of artificial intelligence, barely conceptualized five years ago, has now expanded enormously to add to the prospects and vision for the second stage, which we'll be proposing to you today. Next slide, please. So the impact in terms of publications is an easy thing to measure. You can see in the figure to the left the number of publications increasing truly exponentially into 2024 and this year just beginning. It involves some very high-level, high-profile publications that have provided recommendations for how to study and detect senescent cells given their remarkable heterogeneity, molecular cellular heterogeneity, and then the use of techniques such as spatial mapping of cellular senescence and the that it creates.

And the next slide, please. So, a summary of the planning activities that have gone into the second phase. Here, we used focus groups that involved consortium PIs from the first stage itself, as well as working group members, expert panels convened, and program consultants. The summary was that we need to define the biological relevance of the senescence heterogeneity which appeared in this first phase and understand in terms of the mechanisms that mediate cellular senescence. All this is a guide to senotherapeutics, that is, the way in which manipulation of senescent cells can be used to therapeutic advantage. The importance of developing preclinical models in which the validation of interventions to affect senescent cells can be studied. We need to study senescent cells not just in human normal tissues, but in the context of diseases as well, see what aspects of senescence and senescent cells are pathogenic.

As I alluded to, developing cutting-edge tools, including AI for senescent cell signatures and predictions. And then importantly, too, in the context of the Common Fund and our broad data initiatives to study the enhanced integration of SenNet with other single-cell consortia in the Common Fund and without. Tumor atlas, the human biological map of spatial temporal expression in normal tissues, and somatic mosaicism in SMAHAT. All of these in a common data network which allows the optimal cross-information and leveraging of these several initiatives, including SENET. Next, please. So, portfolio analysis was part of the survey of where we've come from. From 2015 through 2024, in these years, if we looked at the topics which were subject of CENET stage one, so cellular senescence, single-cell spatial tissue mapping, Of the 29 awards from NIH in that time, 22 were in CENET.

Let's get an idea of what a profound impact this initiative has had in accelerating research in this area. The same holds true for the other areas of research around senescence. So already, this CENET has performed its initial task in providing the field with a dynamic beginning, the tools, and the databases on which to proceed. Next, please. The analysis and input of various expert convenings concluded that said investment is needed first to understand the heterogeneity beyond what was expected, heterogeneity in terms of biochemical signatures at a cellular level, the biology of senescence at a single cell level, again, as I mentioned, in both normal disease states. To uncover and validate biomarkers that can be used in both preclinical and ultimately in translational and clinical models, develop the tools and technologies to do so, and to integrate the results of stage one with what the mapping efforts will be in stage two to generate a searchable atlas of senescent cells.

Next, please. So, CNET goals and initiatives. The goals are to understand the biological relevance of senescent cells and all of its heterogeneity, to identify and validate diverse senescent signatures in human biospecimens, and to reform serotherapeutic strategies for human health, again, based on the finding that The senescent cells and their manipulation animal models seem to have impact on multiple diseases and conditions, and so the interventions on senescent cells might indeed have impacts on multiple of the contributors to human health. The stage two initiatives will be the discovery, mapping, and validation centers. The senescence technology projects will further develop technologies needed to study senescent cells in vivo as well as in vitro, and a data coordination and integration and

organization center to make these maximally available and leverageable in the broad research community.

Next, please. So, the first initiative, discovery and mapping, there'll be a series of mapping validation centers. Which will use state-of-the-art techniques, many of which have been developed by the first phase of this initiative, to define organ-specific phenotypes and their function in both health development and in disease conditions, and importantly, to identify preclinical models which allow the perturbation, induction of senescence, modulation of senescence to test and validate serotherapeutics as strategy towards their eventual translational and clinical application. Next, please. Second phase, to use integrated systems biology approaches that leverage multiple scientific disciplines that will bring to bear all of the findings from this basic science to advance current understanding and relevance to senescence heterogeneity, to develop technologies and multi-scale models to determine cellular senescence, and importantly, in vivo outcomes, to use developmental and computational tools such as the AI that I've mentioned several times in carrying out this translation.

And next slide, please. The third component, Initiative Three, to have a data coordination and integration center that will make available the outcomes of these data to the research public. And as I noted at the outset, in collaboration with some of the other cellular large-scale data initiatives that are in progress, all in generating interactive atlases that will maximize the impact of these several efforts. Next, please. The proposal meets Common Fund criteria, remains novel, and its novelty expressed by the way it's contributed to the field already, has transformed the idea of moving senescence research forward into therapeutic translations, has catalyzed its work, as you can see, by the enormous impact that the SENET studies themselves have had on the field, is driven by the same goals that motivated the initiative to begin with, and will synergize with many of the missions across NIH.

institutes, centers, and offices across diseases and conditions and across the entire lifespan. Next, please. So, the Senescence Sennet Stage 2 budget illustrated here. The first component, the discovery and mapping and validation centers, approximately 8 to 10 of them at about $2 million each for $20 million per year for the five-year duration of the proposed extension. The technology centers. Approximately a million each, another six to eight of these centers, and then a coordinating center of $3. 4 million. So the overall proposal with administrative expenses is approximately $30 million per year for each of five years. Next slide. The deliverables will be a curated and searchable atlas or a plural atlases of biology and health and disease, improve preclinical models to accelerate translation, and innovative tools and technology including those of computation and AI to help to predict biological outcomes and advance of the clinical testing of these senescence interventions in vivo.

Next, please. Action, then we're asking of the council is to consider for approval extension of this concept. From a very productive phase one into the second stage or Stage Two of Sales and Essence program, and be happy to address any questions you might have, and thank you for the opportunity to talk with you. Thank you, Richard. And I must just take a quick second to apologize for misspeaking during the intro. The adjective 'new' should obviously be applied to

me, and not to this program. And so I really appreciate you giving us such a detailed overview of the transformative impact that it's already had, and the proposal to move to Stage Two. So, Dr. Lloyd, would you please share any comments with the council? Sure, thanks.

You know, in the interest of time, normally I would provide a summary of what Dr. Hodesar presented, but I think we all get it. And just to cut to the chase, I have a few questions, if you don't mind. First, can you clarify for me, because one of your slides shows portfolio analysis from 2015 to 2024 associated with SendNet grants during that time. So I need to get clarification. Normally, common fund programs are 10 years in length. Have you already had 10 years for Stage One? And this is now the next five years, another five years? Can you explain that slide? Yeah, thanks for the question. I apologize. I see the confusion in the slide. The Senate initiative began five years ago. And the proposal is for an extension of the next five years.

The longer time frame you saw there was the time frame over which literature was surveyed for topics related to CENET. To illustrate that, over that entire 10-year past history, the CENET-supported studies were responsible for the vast majority of research funded in that area. So there's been years of research, but very little of it active, that preceded the five years of stage one of this senescence program. Okay, thank you. Thank you for clearing that up. That was a major confusion on my part. The second thing is on one of your slides, you showed the second next stage one impact, but it appeared to me there was really no complete data set for any of the tissues that were studied. Was that the goal of the first phase? It looked highly variable.

So I wonder if you could comment on that. Yes, so the slide illustrated the number of databases which were published, as well as the number that were under now QC or quality assessment. In these first years, the success has been to generate these large databases and provide their ability to the public now for full analysis. So the data are so extensive that at the end of five years, there's been extensive collection. The analysis is just now being carried out by the multiple omics you saw in those columns. So the specimens are collected, and now the in-progress are the multiple omic dimensions or strategies. Okay, so that table is therefore incomplete because the analysis continues. Correct. Because my concern is that unless you have a complete dataset for all the tissues that will be in the first phase, in which you're developing biomarkers and you develop new tools,

you kind of need that to move on to the next phase in which you're looking at biological networks in both healthy tissue and diseased tissue, and so on. Very well taken. And in fact, to be even more straightforward about it, the phases are dynamic, aren't they? So we'll continue to have more and more analyses with the assays we know and the assays that will be developed. And as we have increasing information, that will all feed into the ability of phase two to translate that into next steps of translation and clinical application. Okay, lastly, a question on the science then. There's obviously a focus on senescence, but I was curious as to whether there'll be any type of investigation into the relationship between a cell entering senescence versus one that

enters apoptosis, which obviously is the death of a cell, it's irreversible, versus a cell that enters quiescence, which is a reversible process, whereas senescence is irreversible.

I wonder if there'll be an analysis of that and finding ways perhaps or explaining mechanisms of how a cell may potentially move between those different phases. That's a great question. And there is a lot of active research being proposed and being funded addressing just those questions in a number of cell types. So, cellulose in essence was initially defined as irreversible. You may note now more oftenly it's talked of more as durable because there may be conditions under which it can be reversed. Apoptosis, as you said, cell death is by definition irreverisible and quiescence yes is a stage of relative inactivity but which is more easily reversible cellular senescence is not a stage of dormancy and perhaps it could have emphasized that more but the the physiologic metabolic activity of senescent cells for example the secreted component, so-called senescence secretome, is the mediator of the activity of those cells.

They don't just stop dividing and sit there in their small numbers. They're highly active. Quiescent cells are more commonly regarded as cells which are truly functionally quiescent, but in a reversible state of quiescence. And as you point out, the determinants that protect senescent cells. One of the characteristics of senescent cells, in fact, is they are resistant to apoptosis. And one of the strategies for eliminating those cells has been to block the pathways which protect them from apoptosis. So there's more is known about the choice points between death and prevention of death and preservation of the senescent phenotype. Thank you, Dr. Hodes. So, Phase 1 looks like it's been very, very productive, very successful, and I continue to work on some of those datasets.

The tools that were developed are very rigorous and will be applicable to the second phase. Dr. Hodes, you presented very strong justification of why this continues to meet the criteria for common fund programs, so I would support the extension into Phase 2 of this program for another five years. Thank you. Thank you for the questions and for the chance to discuss with you. Thank you. Dr. Manley, would you like to add any comments? Yes. Hi, Richard. It's so good to see you again. Great to see you. I am going to put my camera off because I've been having some connection issues today. And I am going to ask, some questions that you may find a little irritating, I'm afraid. They're very general. I mean, I am in favor of this science.

I agree with Dr. Lloyd that it is rigorous that you've made by evaluating some of the challenges that came up in stage one. You've planned your second stage, I think, thoughtfully and appropriately. But I think I need more information about the criteria for continuing any common fund program beyond the first five years. So one example of my question is, What's the rationalization for keeping Cennet within the common fund? In other words, how is this better than IC-driven programs? How has the cost effectiveness of Phase One been evaluated in the context of its downstream impact? You spent some time discussing with us the catalytic and transformative criteria of common fund programs. My question to you is, how will the acceleration of senescence research be measured by this program, as included in your slides, send net grants in that, but is that really how we should be measuring how a common fund program accelerates science in a particular area?

Is that it it funds grants within its program and then my final question is, how has the Send Net program benefited vulnerable populations, patient groups, and how has it been taken up by a representative range of institutions? And I'll put these questions in the chat because I know it's a lot. So I'll try to get through them, Jen, as you pray. The first was an important general question. When should a common fund program like SEMNET be extended? How do we know it should be extended rather than having completed its goals? And it's a challenging question and it shouldn't be taken lightly. I would say in the case of SEMNET, as I've illustrated, we've learned a great deal about the heterogeneity of senescent cells we didn't know before from tissue to tissue and in different settings.

We have the data sets that are extensive but not complete. And if the goal is to provide atlases, which were expressed explicitly as a goal, that then should be easily accessible and usable by the research community. That's the state at which I think a common foundation such as this will have accomplished its mission. I think without the second stage, we would have been successful in provoking more research, but not nearly as extensively as would be the case after a second phase, completed atlases, well annotated and accessible to the research community. Related. Your second point, I think, was about how do we measure success. And clearly, just the fact that we have funded publications by a common fund initiative itself are not sufficient.

One, A relatively proximate outcome would be when the field takes off and now research in the field of a common fund initiative like Cennet is being supported by grants outside of Cennet itself. I would expect to see in these next years a growing amount of this, even more acceleration as we approach the end of what I hope will be the second phase, when we have atlases of help to the public that allow investigators to enter. A metric of success we've used, Jen, I think you've seen in some of our other initiatives, we get to the stage where publications are coming from investigators who were never even funded by the initiative itself, like CENET. I think that's a criterion that would catalyze the field, and we can step back and be gratified in that.

And your third and final question, high in mind for all we do, how this benefits people, populations, the full scope of the American global populations, the fact that in the preclinical animal models, that the reversal of senescence and elimination of senescent cells has shown promising impacts on varieties of age-related pathologies gives us strong confidence, though we never know until the end product, that by intervening on senescent cells, we'll be impacting many aspects of aging, the precursors to many conditions and diseases, which affect very diverse populations. So there's no question the basic science seems right. Relevant to those diseases and conditions which impact diverse populations, the final mountain to achieve and to climb, of course, is to translate into interventions which then can and will be applied in those diverse populations that we are talking about.

Until that, we don't have the final success that I think we aspire and feel is a promise yet to be achieved and demonstrated by the initiative. So I think those were your three points. Just one more addition to the last one, which is, have the CNET grants been awarded to representative

set of institutions that are eligible for NIH grants? That's a good question. I mean, representatives is a challenging part of the question. I don't know. Multiple awards to multiple institutions. They're generally research one institutions. But fair to take a look. And, you know, if there's a second phase coming up and we're looking again at the outcomes of a second advertisement. I should say that the plan is for Stage Two, not to limit that to just those successful sites in the first phase, but very explicitly to hope that more and a broader spectrum of institutions will be capable of generating proposals.

And I would also point out, I think it's been a rule rather than exception, that these proposals have come from consortia of institutions. So each of the individual awards itself is from a consortium, something to be recognized. And another aspect of the CENAT activities that was not stressed in the science aspect was, I think, a very successful model of developing a program for new and young and emerging investigators in summers through training to experience research in the programs very explicitly, Jen, intending those to be a next generation, an inclusive generation of people who may not even have been in many of these cases at the institutions who got the first award. So I think there's been a very conscious effort to broaden the research community that is likely to be involved in the second phase of research and beyond, and credit goes even beyond the research accomplished by myself to the work of this consortium.

Yeah, and Richard, I'll just add on that last point. This is Carolyn, to say that we are also doing that not just within SendNet, but SendNet also participates in our larger Common Fund data ecosystem. And we have some activities within that data ecosystem, including RO3 opportunities for people to come in and use the existing datasets from SendNet and other projects, either individually or together, as well as some training and education outreach activities within that program that also help broaden the scope, not just who's getting some Common Fund funding to work with SunNet and SunNet data, but also getting the exposure and the ability to sort of use that Common Fund resources. Thanks, Carolyn. And I might ask, Carolyn, if you, just to ensure that we've addressed all of Dr.

Manley's questions, if you maybe want to expand a little bit on sort of the rationale for keeping SunNet within Common Fund and how this type of a transformative cross-cutting research program is really best supported by a common fund that allows you know the common fund as a program allowing us to work cooperatively across many different ICS rather than having that be driven within an individual or even with a couple of ICS. For me, from a biological perspective, cellular senescence affects so many different endpoints and so many different pieces of biomedical research that I think that that provides you know some strong support to it, but I wanted to ask if there was anything else that you would like to add on that particular point.

Yeah, no, I think I'd very much build on what you said and also Dr. Hodes' thinking about this program, you know is the working group comes from the different ICs. And if it transitioned and we said, 'Oh, this is mostly of interest to aging; I'm not insulting my NIA colleagues, but I'm saying we'd then lose the perspective that having this as a common fund program with that trans-NIH working group and that NIH-wide collaboration bringing in the expertise across the

different areas and the realization of how to think, particularly in Phase Two where there's this disease focus, how to really integrate it in with the subject matter expertise and perspective of all of the impacts across NIH. So it is one of the things that we ask, and, you know, Dr.

Hood has laid out, this tying into those five criteria and the synergism and the sort of applicability across NIH is a critical thing that we ask in considering the continuation of a program within Common Fund as opposed to making it something that would be transitioned into an IC. Because we have had Common Fund programs that have done both. And so, in this case, I think it's really the applicability of this to activity across the entire NIH mission that makes it benefit from that NIH-wide coordination and perspective that comes from Common Fund programs. Thank you, Carolyn. I'll just circle back and ask Jennifer if your questions have all been addressed. Yes. Yes, they have. Thank you. Okay, fantastic. Do other council members have any other questions or comments?

If so, please raise your hand and you'll be recognized and asked to unmute yourself. And if not, we will proceed to a vote, okay Francesca go ahead all right great thank you I will be calling for the vote and that will read 'I have a motion for approval of the common fund concept clear in stage two entitled and sellers in essence Network send' that program To support the motion, please say 'move'. So moved, and I see it, and I see the second. Is there any additional discussion at this point? I see one hand. Is that from before Monica? Oh, you're muted. I meant yay. I didn't mean nay. Oh, okay. Sorry. Thank you. So, if there is no more discussion, we'll do the same procedure over. I turn it over to Christina for the hand-raising vote. Thank you, Dr. Greeter. As a reminder, only council members should participate in this vote. This is a vote on the motion for approval of the presented concept clearance. Please raise your hand to vote aye.

I see 13 hands. I see 14 hands. Please raise your hand to vote aye. All right, thank you. I see 14 hands. Please lower your hands and we'll move to the next vote. Please raise your hand to vote nay.

Thank you. I see one hand to vote nay. Please lower your hands. Thank you. Please raise your hands to vote abstention.

Thank you. I see one hand. Please lower your hand. This concludes the vote. The motion, as stated, has passed. Great. Thank you, Christina. Back to you, Nicole. Great. Thank you so much, everyone. Okay, moving to the last concept of the meeting. So this is also from the Office of Strategic Coordination and presented by Mike Chang, the NEI, the National Eye Institute Director, and Bruce Tromberg, the Director of the National Institute of Biomedical Imaging and Bioengineering. So, the presentation for this new concept, putting myself out on a limb here, I'm pretty sure that this is right, entitled 'Precision Medicine with AI'. By integrating imaging with multimodal data, so the primed AI program, will be followed by comments from the two assigned council member discussants, Drs. Kevin Johnson and Dr. Linda Chang. So Michael, Bruce, turning it over to you. Can I request a five-minute break or otherwise I won't be here for the next five minutes?

Yes, let's take a five-minute break, and we will reconvene at 3:33. Thank you, everyone, for adhering to the five-minute restriction for our break. And so now we will jump in to our last concept presentation. So, Michael, Bruce, I'm going to turn it over to you. Great. Thank you. Thanks to all of you for sticking with us through this presentation, or at least starting the presentation. So I'm the director of NIBIB, the Imaging and Engineering Institute. And Mike, I don't know if you're on. Did you flash your camera on? I am on. Michael Chang, director of National Eye Institute. Excited to be here. Yeah, Mike is director of the original Imaging Institute, the very first one. And we continue to see that move forward. So we'll be presenting together.

This is a new concept, although one that certainly has a lot of discussion and popularity in our community more broadly. So, let's go to the next slide. So, we'll be presenting four basic sub-goals. We'll give you an idea of the details of each of these and the origin of breaking the structure down into these. We anticipate in the five years funding about 90 awards spanning multiple award types, reflective of the kind of community effort that we really need to encourage and build in order to have a successful concept. Next slide, please. So, Mike and I are representing a really amazing group of people. This is about 50 different individuals contributing to this entire concept very enthusiastically. First, our working group co-chairs, Susan Gregorick from the Office of Data Science, Richard Hodes, who leads the NIA.

You just listened to Richard in his presentation. And Walter Korchetz, who leads NINDS. We've worked really closely with Common Fund staff, Chris, Sahana, Caitlin, and David. Our main program coordinators are program officers, program directors from three different institutes, Sangeeta from NEI, Mike Espy from NCI, and Chris from NIBIB. We've also coordinated, of course, with grants management and CSR and our working group program directors. There are about 35 of them from 19 different ICs, institutes, centers, and offices, really reflective of the broad appeal of this initiative that really cuts across so many different institutes and programs. Next slide. So this is the imaging representation, kind of the iconography of the entire concept. And, of course, we'll get into details in every one of these components.

But all of you who are familiar with medical imaging, radiologic imaging, first of all, there's been enormous activity in the development of data science approaches, artificial intelligence-based techniques in radiology. Of the more than 1,000 or so algorithms that the FDA has authorized in terms of software as medical device using AI and machine learning, about 75% of them are in radiology. Pathology also presents unique opportunities for using data science approaches for extracting deeper information content. Camera images, we say camera, but any way or form; of raster scanning a sensor or single point imaging detector to get optical imaging information from endoscopy or ophthalmic scanning, dermatologic scanning, a variety of different approaches there. All of these methods have enormous information content.

So, if you look at what is typically delivered in healthcare, a clinical impression from a radiology report may contain a few sentences of information. Kilobits of information content, but our research communities in each of these imaging sectors have really been pushing the envelope to extract what is closer to the true data size of each of these imaging approaches. Megabytes, gigabytes, terabytes of information content. There's enormous activity both with the

development of advanced data science approaches and the combination of these methods with clinical approaches and clinical information content from lab test results, from clinical data, and impression reports that really potentially can dramatically increase the power in the information content of all our imaging studies. But imaging tends to be somewhat siloed.

Clinicians who are guiding patient management don't really understand all the different technologies and approaches that are really beautifully being developed by the research community and could potentially inform how to optimize precision medicine for patients. So, this is the essential challenge for us. There's an enormous amount of research that we support at the NIH and many of us have been deeply involved in for several decades. This spans from radiomics to AI-based techniques for extracting unique information content that previously was invisible in medical images, but with new techniques for background suppression, enhancement of contrast to background, and correlating what we see in an image with all of the lab results and the clinical data; this is a very, very vibrant field of activity. But it is very far off from what we're seeing in clinical practice.

So our fundamental challenge is to take this multimodal data and integrate it in such a way as to improve prognosis and diagnosis for patients, do it in a validated way, verify algorithms that are being developed, and distribute them fairly and equitably for all patients who will benefit from it. So that's far off from where we are in the research community, but we believe this is a unique moment where we can leverage significant advances in many of the different technologies that go into this concept, from the imaging methods themselves, to the data science and computational methods for extracting information content, to multimodal types of learning strategies that integrate very beautiful imaging types of approaches with our clinical information content and lab test results, which tend to be lower bit rate information, but combined with imaging where we could potentially extract very, very high-megabyte/ gigabyte information content, we can do things, I think, that are very unusual and powerful and transformative for patients.

So next slide. One of the things that we wonder about all the time with common fund programs is, are we doing this already? And the answer is kind of yes and no. So this slide, the top plot, shows the expansive growth of AI and ML deep learning techniques across the NIH. More than 6,000 Type 1 grants integrated over that five-year interval from 2019 to 2023. But once you start to narrow this down and look at this in combination with clinical imaging, we reduced that only to about 2,000 Type 1 grants integrated over that entire five years. And then if you look at how these will come together with precision medicine, it's even fewer. The grant total is in the hundreds. So this says a couple of things.

There is a significant amount of interest and investment in the fundamental techniques that are driving AI, machine learning, and deep learning, but they're kind of siloed from one another. So we have infrastructure and capacity all around the country in these core technical areas, but we don't have a cohesive structure to bring them all together. So this suggests to us that there are key opportunities here for federal and non-federal partnerships. That could make this initiative quite powerful. Next slide, in our next step of really evaluating is this something unique, is it just

a figment of our imagination? We just think this is important, so therefore we want to move it forward. We did a public RFI and held a strategic planning workshop March 11th and 12th; so both of these provided enormous response and information content.

The strategic planning workshop: over 1,000 participants engaged. We hadn't announced the initiative at all, just the ideas behind the initiative. What were these key ideas? Based on the public RFI, our team really extracted four major themes: imaging and multimodal data integration, AI algorithm and tool development, clinical implementation, and building trust and coordination. And these are the four foundational elements of our program. And if we go to the next slide, Mike will take it from here and expand into all of those elements of the program. Yeah, Bruce, thank you. So basically, this slide talks about basically these unmet needs that follow naturally from what Bruce just talked about. I'm just going to take you through these bullet points quickly.

If you look at the first bullet point and the third bullet point, they basically talk about an unmet need going from single modality data to multimodality data and linking those data across the different scales from molecules up to patients to populations. The second bullet point here talks about addressing these unmet needs and gaps involving, for example, interoperability and harmonization that are going to move us toward advancing AI-driven precision medicine for all Americans. And the bottom two bullet points talk about real-world implementation. Getting these AI tools into clinical decision support tools that could be used by clinicians using electronic health records and building all those relationships among the stakeholders, patients, clinicians, data scientists, that are going to be needed to really move the field forward. So if you can go to the next slide, please.

In this slide, what we really talk about is moving from blue sky to make it a little bit more tangible. So here, we describe a series of NOFOs that are intended to address four iterative subgoals, and these goals are color-coded. So going from left to right, at the upper left, there's integration of image data together with multimodal data. Okay, so that's well, the multimodal data could be clinical data, genetic data, multiomic data. So then up in the blue on the upper right is building those AI algorithms and tools. And those tools could be used to do things like clinical diagnosis, patient management, prediction of future disease. So then going down to the lower left, clinical implementation, this is all that real-world implementation that we talked about.

And in the green at the bottom right is trust. And you'll see on the diagram the trust encompasses everything. And, you know, what do we mean by that? Program cohesion, adaptability, scientific validation and rigor, and transparency. Okay, so just keep in mind that these concepts don't work in isolation from one another. Like, for example, there's not going to be a yellow NOFO and a blue NOFO. In reality, these subconcepts are pretty heavily interrelated. And so what I want to do, if you can go to the next slide, what we're doing is taking all these circles and basically flattening them. And this is going to be a little bit even more tangible about the actual NOFOs. Same color coding as on the previous slide. And going from top to bottom, the data integration is in yellow.

And here, there'd be three sets of NOFOs that we would really propose. One is what we're calling a playbook of standardized frameworks. And here, the way this would really work is that these playbooks would describe essentially best practices for building multimodal AI systems for different use cases. And so investigators could use this playbook to get help with a range of challenges, you know, from best practices for validation of AI algorithms to identifying indications for use for clinical implementation to navigating regulatory hurdles. Academic industrial partnerships and that really gets into what Bruce was talking about about building collaborations and getting stuff into the real world, and you know the last of these is a set of NoFo's to develop modular software tools.

So there would be a lot of tools, and we would intend to fund about 40 projects in this area. And some of these tools would be to – so the idea is that they would be reused by a lot of different groups around the country. They could be used for multimodal data integration, for evaluating the robustness of models, or to basically develop better user interface design widgets. So a lot of these modular software tools. If you can push the button once, please. The red here refers to those clinical implementation and testing phase. And here, there's a single NOFO that's called the model-to-clinic NOFO, which is the single biggest one in this project. And I'm going to talk about that in the next slide. And so, if you could push once more.

And the last of these is that there's the trust set of NOFOs. And you notice here, again, that it encompasses all the other projects. And here, we envision this as a series of three centers, basically. One is a validation center. For doing verification and validation independently of the tools that are developed through Primed AI. The next set in the middle is a logistics center, and that's basically going to do all the program administration and teaming support and engagement with stakeholder communities that's going to be so important for a project like this. And lastly, on the bottom right of the slide is communication curricula NOFOs. And these are basically going to be NOFOs to develop strategies to build communication and trust among, you know, data scientists, clinicians, and patients.

And we think that's really going to be important for a project like this. Okay, and if you can go to the next slide, please. In this slide, what we really give is more details about how this model to clinic NOFO, you know, would look. So again, this is the single biggest set of NOFOs that we're proposing in Primed AI. There'd be about 10 of these that we would fund, and the total investment would be $50 million over five years. So we envision this occurring in two phases. Phase one is developing the tools, and phase two is testing, what we call ancillary clinical testing. So, again, it integrates all the yellows, the blues, the greens, and the reds from the previous slides.

So, in terms of yellow, the data integration, you know, the data could come from existing repositories of images and multimodal data. The data could come from retrospective clinical trials. And, you know, we would develop tools to integrate those data and make them interoperable. And then moving to the blue, we would build AI algorithms to solve defined clinical problems. And our anticipation is that we would have essentially a go-no-go funnel. All these tools that are developed, the ones that would meet certain benchmarks based on

preliminary testing, would pass and advance to phase two, which is ancillary clinical testing. And if you could advance once, please. On the slides, um, the way that this would work is: The red bars here.

We would identify mechanisms to perform ancillary clinical testing of these AI algorithms, and they could be tested in academic medical centers, in community hospitals, or they could be used, they could be applied, for example, for existing industry-funded clinical trials where we would define new secondary outcome measures that primed AI algorithms could apply to. Okay, so, you know, what we're really trying to do is to create opportunities to get this into the real world. And at the bottom in the green, there would be an independent model testing that would be done in coordination with that validation center, one of those green areas. And so I really want to emphasize that I hope it comes across that the design of this is really meant to respect the fact that AI is really rapidly evolving.

It's a dynamic field. And we want to make sure that this ecosystem of primed AI projects leaves us with the flexibility to evolve this concept as the field evolves. We really want to be agile and nimble and give us the flexibility to pivot as the field changes. If you go to the next slide, please. This next slide basically summarizes the budget that we're talking about. So it's $120 million total spread over five years, and all the NOFOs are defined, you know, that we showed on the previous slides. Starting from the playbook and academic industrial partnerships, you'll notice the model to clinic NOFO is the biggest one, 10 awards, $51 million. And down at the bottom are those trust, you know, validation center, logistics center, and communication criteria.

If you can go to the next slide, please. These are the deliverables, and we're really excited about this. Best practices for AI-based precision medicine through integrating imaging and multimodal data, developing a set of innovative and reliable tools, and lastly at the bottom, and really importantly, developing a series of durable relationships that are going to sustain the field and hopefully expand it in the future. If you go to the next slide, which is our last slide, these are the take-home points that, you know, Bruce started out by saying that we're really excited about this project, and I would just finish by saying that. You know, we've got a lot of people at NIH from different institutes involved and, you know, really excited about this as a common fund concept. AI-supported translational impact for patients.

Trying to advance culture change in clinical practice by enabling precision medicine strategies at a large scale and getting input from all stakeholders, and basically accelerating use of multi-scale digital biomarkers. So with that, I'm going to stop. Thank you for your attention. And, you know, Nicole and Francesca, may we turn to you to lead this discussion? Thank you both very much. So I will pass it over to Dr. Johnson. Would you please share any comments with the council? I would be pleased to. First of all, I want to applaud you both for developing this concept and really thinking about it as an ecosystem for the development and adoption of innovative AI-based tools. Uh, the gap that was identified in the research related to integrating imaging and multimodal data is definitely one that resonates with the community at large, as well as in the Bridge to AI investigator community.

I did notice that in the gap there's a couple things you didn't discuss; I'm going to come back to those um My presentation is going to be a little bit scattered because it turns out that the slides needed to be talked through, not shown, as I think you probably know. And so now that I've heard it, I wrote some notes that I wanted to make sure I included. First of all, the idea of the four sub-goals that are summarized by the team are exactly the high-level aspects that would be needed to have translation and impact from things like precision medicine using AI. I would note, though, that every single one of the words that's bolded is frankly up for debate in terms of its overall utility.

So, I think it's going to be important to ask those as questions, in my opinion, not as assertions. The best example of which is federated learning. While federated learning has a role in privacy, it also has opportunities to stifle innovation, as we've learned even from things like Odyssey. So, you guys know that, and I just want to bring it out to our group that Many of the words that you'll see in the original concept probably should be discussed as individual ideas, and I'm sure they will be as this concept kind of evolves a bit. The other thing is I didn't quite see enough about what was learned from Bridge to AI. I went through the RFI. I saw a little bit, but I still realize that Bridge to AI is ongoing, but it appears that they have a lot of lessons.

Some of them are in here. And they have been iteratively applied to what to this proposal's requirements, but some of them are not. And so, I just thought it would be useful to make sure that you've exposed that. And if I missed something, I apologize there. It seems to me that the communication curricula and the logistics center are really important aspects of this trust dimension. As I was looking through that and also being very sort of thoughtfully considering what Dr. Bhattacharya told us today about the big ideas and data, I wonder to what extent the trust components need to be thought of as sort of a public-private partnership right from the very beginning so that, in fact, we can get involvement of stakeholders who are likely to help scale in industry as well as in academia.

Without that, I wonder whether even though you've put a lot of money into that particular set of three programs, I wonder whether it's sufficient. Without having something that looks more like a public-private partnership, especially given the work that's going on with AI Assurance Labs and many of the other initiatives that are out there, including some of the work that the FDA under Dr. Califf started that I'm sure will continue. I also note that there are some multimodal data that are not included that I would personally love to see included. There's very good data now to suggest the use of unstructured text. Perhaps you included it, but you didn't explicitly say it. I didn't see anything about audio signals, and I didn't see anything about video.

And I think all of those are not yet explicitly mentioned, but all of them are being actively funded, both at the NSF and at the NIH. The budget seems appropriate for the most part. I'm curious how modular software tools and R03s will progress to R01 level funding. And in particular, again, thinking about the current NIH director strategy, these are big ideas. And I'm wondering whether there's different mechanisms that could be used, whether it be one of the UH mechanisms or other mechanisms in addition to small grants and R01s. Is there an expectation of institutes that will pick up the funding requirements to enable these projects to get all the way

to clinical trial? In other words, if I get an R03, is there anything you guys can do to help guarantee that successful projects get all the way to trial without having to constantly recompete per some of what we heard about this morning that I think you've heard about?

Or is the idea that modular software tools to address critical gaps in the data-to-models pipeline? That this would not develop technologies that would be useful at the bedside. I believe from what you presented that your hope is that things go from sort of foundational and basic science all the way to trial through this set of mechanisms. But, if so, I think it would be great to make sure the concept kind of has explicit language about some of the ways in which that transition could be improved for groups who are funded through this mechanism. Those are my main comments. I applaud you on a big idea. I applaud you on comprehensive thinking, and I'm very excited to see what comes out of this. I'm going to be very supportive. Thank you.

Mike, maybe I could start off. So, talk about high bitrate information content. We need to capture that audio and parse it out through generative techniques. I think you hit so many of the topics that we've been discussing. Maybe, Mike, I'll just jump in on, you know, Mike and I, and the entire group, we're impatient. We see the beautiful basic research, support it, and it's incredible and inspirational, but we are also feeling the gap between the actual clinical practice of applying all of what we are finding in imaging studies across the board to management of patients. And what we've done in NIBID, so we're bringing the cultures of our institutes and the skill sets. So I'll just address a couple of these issues with respect to the tools that we can provide to accelerate the validation of algorithms and to move them through the regulatory process as quickly as possible.

So in many of the programs that we support at NIBID, we have very deep partnerships and a very strong track record. With engaging FDA right at the beginning. And we're doing this in one of our sort of premier imaging databases, the Medical Imaging Data Resource Center, or MIDRC, which integrates. It started in COVID, and it's pivoted to cancer. And it's an example of how we can develop algorithms, validate them, and move them quickly through the regulatory process. It also has explored to some extent the federated learning. And really, you know, we have been trying to identify the key advantages to when things are better moved through federated processes versus databases. They each have their own challenges.

But I think we're in a unique position at the NIH where I think we can recognize and identify the advantages and the disadvantages and provide supportive resources for the validation process, independent validation. And then bringing regulatory into this mix as early as possible so that we can get software as medical devices approved and distributed in very trustworthy kinds of platforms. So, I'll stop there because you covered so many topics, but yes, we do have a whole bunch across our institutes of ongoing ancillary support in addition to partnering with ancillary studies that are being supported across the NIH and even in the industry community that would drive these public-private partnerships, working with industry, working with FDA. This is very, very normal for us, and it's something that we anticipate that we'll tap into very, very deeply because all these tools are so fast-moving, and there's such a high demand and expectation of growth.

Thank you. I'm happy to share my notes, by the way. You know, Kevin, I'm only going to say a couple of things in follow-up to what Bruce said, which is totally appreciated your comments. Every single one, I think, resonated with me. I think one of the things that we really tried to leave flexibility in this project design is to evolve the project as the field evolves. Like, we didn't show a Gantt chart about the different entry points of projects, but I'm hoping that you mentioned a comment about federated learning in particular, and I think there's a good chance that the field will look different in 2027 compared to what it looks like right now. And I hope that's going to be accounted for in our project design.

Kevin, you mentioned something about multimodal data and things like unstructured text and video. And I completely agree. You know, just on a personal level, you and I had a great conversation when I was in Philadelphia, you know, about a year ago, and I loved some of the stuff that you're doing with that. And I think that there could be a lot of, you know, I agree that I don't think the only form of data is a doctor or nurse, you know, checking a checkbox. Or using a so-called 'dot phrase'. So that would be, you know, fabulous for so many reasons. And, you know, there are many things that, you know, I've personally learned from Bridge to AI.

You know, better ways to do teaming, the importance of data, you know, the importance of standards and how everybody likes standards, you know, as long as they're my standards, and you're not using somebody else's. But one or the other, I completely agree with what you said about public-private partnerships. And that's sort of the spirit of these academic-industrial partnerships. But, you know, as Bruce said, maybe we need to do more with engaging FDA or the payers, okay, up front about this. But, you know, ultimately, one of the things that I personally learned was that bridge to AI is not enough to advance the field. And so, hence why we're here. So, thank you for all that. And I'll stop. Thank you. Mike, if I could just two quick add-ons to that.

You know, from Bridge to AI, Kevin, you mentioned the audio data, which we're so excited about. And in fact, you know, that could be one of the very most beautiful standard and easily accessible standard data formats to be able to integrate into this. We're certainly expecting big things from that program in Bridge to AI. And, in terms of the RO3 mechanism, this is a really ongoing discussion and debate amongst us. R03, even though it's a lower barrier to entry, is not necessarily a fast turnaround time mechanism. And so, we're exploring approaches that we've pioneered in NIBIB through the Rapid Acceleration of Diagnostics Technologies program. And Mike had mentioned the innovation funnel in his presentation part. And so, we are absolutely considering that as a way to get funding to developers very, very quickly in unprecedented time frames, you know, a matter of weeks.

But also build teams around them to optimize the concepts that are proposed and provide them with additional resources for doing better with the technology moving it to markets potentially if it's being commercialized and partnering with the FDA so. These are all topics that we feel we can draw on because of our collective experiences across this amazing group of 19 different institutes, centers, and offices. Thank you. Okay. I think, well, I'm the other discussant, so do

you want me to mention a few things? Perfect. Yes. Thank you, Linda. I was just about to call on you. Okay. All right. Well, thank you again for this presentation. And you guys, I mean, Dr. Chang and Dr. Trump, you guys have, And your team of 50 people have done an amazing job of, you know, delineating some of the all the different points and the things for this concept.

I think it's a great concept overall. And I agree with everything that Kevin mentioned already, too. So I'm not going to reiterate those. But I did. So I'm just going to mention a couple problems that I see with feasibility. And I'm sure you thought about them and you started to talk about some of them already. And also, I thought what you are proposing is actually so similar to what the new NIH director just presented. Did you see this morning? He has this real-world data platform that he mentioned. It's like the same thing as what you're trying to do, except I don't know if he meant to apply that just to autism or to any disease. You should go back and look at that slide. It looks exactly the same as what you're planning to do.

Maybe you can team up with him and get more funding for this. Anyway, so my two areas that I want to bring up regarding possible feasibility issue. The first one is Has to do with the input data, right? So you already saw from the executive summary from your RFI that the first item, they emphasize the importance of standardization and data integration, and addressing the variability in the imaging acquisition and data harmonization. Because I can tell you, I'm involved in this big multicenter study, 21 sites for the ABCD study. And we have like the same protocol, this identical three Tesla scanner across all the sites. And it's the same, you know, already optimized imaging protocol, but we have different vendors like GE and Philips and Siemens.

And even with that, it's so hard to harmonize when we end up having to like throw out data in order to get reasonable results to minimize the variability. So, you're going to be if you're going to be working with like clinical data from everywhere, you know, you're going to get EHR, you know, electronic health record. From different hospitals, from different clinicians. Everybody, you just mentioned this earlier, everybody charts things differently. Like, are you going to develop tools for clinicians to enter the data uniformly, kind of like the way we do data collection with a scientific protocol? That would certainly help, maybe. I don't know. But it just seems like in order for this to work, you will need billions of training data sets. Like the way CHET-GPT was developed with billions of files and websites used.

So, I'm just not sure like anyone or two sites, one or two institutions can actually achieve this goal. And in some sense, developing algorithms to combine the various clinical data sets that you mentioned, the funneling or whatever, to improve medical outcomes, it's a very It's like an applied project because I think a lot of algorithms are already available. You know, because you saw even with your NIH award that there are many, many people developing algorithms, but they just don't apply them, right? So, you need to bring it together. So, it's just finding the data would be very difficult. So, that's my first point. And then, the second point is I think you have very limited budget. I know Kevin mentioned the budget's appropriate.

But if you go online and just look at how much it costs for open AI or some of the AI development in the private and venture funds, I think they invest over $100 billion per year. I

think in 2024, they said they invested $110 billion a year to develop AI tools. And I can tell you most of them are actually for medical applications. It looks like the private money is outspending NIH by orders of magnitude. So I think you need a lot more money to make this to work. I looked up about, I think FDA approved a lot of 900 AI machine learning enabled medical devices last year alone. And so the growth will continue to ramp up. And so, the global AI and healthcare market is projected to reach $ 164 billion by 2030.

So, I think we will need more money. The final point about needing more money has to do with infrastructure, because in order to maintain, you need a lot of computing power. For instance, Chet GPT costs something like this: With OpenAI, they spend $700,000 a day to run ChatGPT. And I talked to some of my colleagues that are doing AI research in radiology, and they said that a lot of people in academia have a really hard time. So, if NIH can provide some kind of computing infrastructure to enable the scientists to, like, some sort of open computing resource that allows researchers to try even middle-sized networks. So, even the smallest LM. LLM network is challenging for most of the researchers in academia. So those are my points.

I just think it might help with what you want to do, but you should ask for more money, I think. Well, Linda, thank you for those. Maybe, Bruce, I'll start here and just say that thank you for making those three things. If I can, to me, it seemed like you made three points, and two of them, input data, garbage in, garbage out, and we need to standardize data, totally agree. Perhaps one of the approaches that we'll take is developing AI methods to help with that standardization and that harmonization. Computing power methods for that, we've definitely talked about this. There's an advisor, the NIH Council, the ACD, has a working group on AI. Both Bruce and I spoke to that. that topic came up in the discussions. So totally agree, totally agree.

Your third comment about budget, I'm not permitted to opine on, you know, as a government employee. So I will just thank you. I mean, if you just look at how much my industry is spending, like what you're trying to do is like a drop in the bucket compared to what they are doing. So it's like, I know you have to start somewhere and also focusing on imaging is really great. I do imaging research, so I really support that. But I just feel like. How much can you do compared to what the rest of the world is doing? So if I may just jump in quickly here, I just want to highlight Linda one of the comments that you made actually I think is really essential to understand that this is, well, this is a really fantastic concept in and of itself as a standalone program.

Inherently, it's not going to function in a vacuum or in a silo. So you highlighted the presentation that Dr. Bhattacharya made this morning and his remarks about this real-world data platform. So we fully expect that primed AI will be one of the sources, the data sources and one of the platforms that become integrated through that real-world data platform, just like the NCATS N3C or the NIA linkage. or the NCIC or you know there are so many existing efforts and data infrastructures across the NIH that deserve to communicate and talk to one another and be joined with other real-world data sets, such as those that Dr. Bhattacharya mentioned, that we are in discussions with our federal partners across the government to access in a secure fashion; and so I think that that will probably provide some of the infrastructure both from the

storage and the compute side that you're a little bit concerned about that you highlighted in your comments around this particular program.

So it will be operating as sort of a piece of a larger vision. I think so, yeah. That's a good point. When I saw that chart this morning, I said that's exactly what this concept is about. But we think it's really a good framework for this broader ambition that everyone has, which is to integrate data that's commonly acquired in clinical interactions and get more out of it. And the imaging community has been doing that by combining physics models with AI-based approaches since, I guess, people started doing machine learning in the 90s. And so we hope to build on that culture, the Quantitative Imaging Biomarkers program that we started at NIBIB and is continuing with RSNA and other external support, the Imaging Phantom Technology program that we've started with NIST and FDA so that we can distribute those resources to our community to help harmonize some aspects of data.

And the general engagement of professional societies like AAPM and RSNA and ACR, especially the physics and engineering side where people are very, very concerned and cognizant of the computational resources that are needed and always worried that these kind of inverse problems that we're trying to solve are ill-posed and are obsessive about trying to reduce bias in the input data that's going in. So we think and we've seen in the past how this combination of cultures can lead to really better outcomes. And in comparison, you know, to the open AI approaches and Stargate AI, they're really moving quickly towards the super obvious or fast commercialization opportunities. They've identified markets. They're moving quickly to that and bringing in more brute force type of large language models and generative techniques.

We see a more refined approach from our community, not necessarily the big commercial markets at the outset, but getting to truths that clinicians are seeking and our scientists are seeking that are relatively low-hanging because we're just leaving so much information when you generate that impression from your radiology report. Oh, my gosh. You know, there's just so much more there. So that's how we'll try to navigate. Between this sort of big, big money requirement and enormous, and you're absolutely correct on an estimate of both the money and the information, you know, the data content that has to go forward. But I think we are in a unique position with our communities where we can make a lot of progress right now in these areas that are not necessarily focused on by the big capital interests.

In Maryland, actually, we just Montgomery County and also the University of Maryland Medical System, they just created a new institute with the medical school. It's called the Institute of Health Computing. And they started with $70 million to start, and then they got the state to agree to give them-this is our tax dollars. So we've continued to fund them for like at the tune of about 6 million a year just to maintain it. And they're doing something very similar to what you are talking about. They're studying with the EHR record and inputting all the data. It's not imaging-focused, but it still does, the concept is the same, integrating clinical with all the labs and everything else they can get together to improve prediction and diagnosis for patients.

So, anyway, you might want to talk to them, too, because they seem to be spending a lot more money on what they're doing. Yeah, thank you. It's called the IHC, Institute of Health Computing. They're actually located across the street from you at the White Flint area. Great. Thank you for the suggestions. Okay, we have several other council members whose hands are raised to contribute to the discussion, so I'm going to turn to Rhonda first. Thank you. You talk about a really innovative idea. This is definitely one of those big ideas, but it's also a huge project. The thing that I fear the most, because this is a direction that many stakeholders are going into already, that if it's not managed well, we'll have a massive fragmentation.

Of all different types of approaches that won't have any interoperability at all and just provide more confusion. And so, I do think one of my questions is, what is the most unique and valuable role that NIH would play in this? And there are some unique capabilities that you have that I think would be very, very important in moving this forward as a national process. I do think that one of the things that you do have in your back pocket is that you can, because of your position, because of how you're funded, that you would have some regulatory navigation skills and credibility. So, that's going to be important to begin to bring in a hone in on what needs to be standard and what isn't.

And you also have the ability to test out through your funding, through others doing it, but having the guidelines or the way of testing something to be able to declare it as a standard in some way. I think that's very, very much so in your area. I agree with the last person who commented. The amount of money in this is just tremendous. I don't see this being a NIH-funded, but I do see that there are multiple investors out there that are in this. But I think with a strong sense of a regulatory piece that is going to be applied to this will help bring some of those investors who want to be in this space to start working with you.

Because I think that's going to be exceptionally important in terms of bringing the continuity, the standardization, and all of that that will allow this to work. Other than that, I take my hat off to you to say this is a huge project, exceptionally important. There are a lot of organizations that are doing this that have lots of kind of data. And I do think there's a way of And capitalizing off of what's been started by, again, figuring out what your role is, your unique role, what you very uniquely are capable of doing that they cannot, and also recognizing that the standardization of data but also the algorithms and all of that needs to be held by something that has tested it out and can demonstrate to those who are participating what is more valuable, what's more valid in the long run.

So, thank you for the opportunity to comment. Robert Hopkinson Thank you. Mike, do you want to start? Yeah, Rhonda, I would just say thank you. I know I sense that I see a lot of hands raised, and so I don't want to talk too long except to say thank you very much. We don't, we haven't met, but I see that, you know, where you're from, and I would love to sort of have future conversations about this. You mentioned a lot of, I feel like you answered the question that you asked in some ways. Validation standards, working across federal agencies like FDA and CMS and other payers, public-private partnerships. And ultimately, we want to try to advance a whole

that's greater than the sum of the parts, not one that's, as you said, fragmented and less than the sum of the parts because it's all confusing.

And I do think that we can play a big role in that at NIH. Thank you. Yeah. And so, just adding on to Mike's comment, I mean, we're going to bring to bear all of the experiences and resources that we've had collectively as our NIH community, and those involve building new capabilities in exactly those areas that you mentioned. So, we have very strong relationships with CDRH, digital health, the OHTs within the FDA, and in the commercialization community where we can bring experts in. To sharpen and refine ideas, and then to validate and test the algorithms that are under development, and get to a deeper understanding of exactly how they work and potential markets for those. So we're going to, we are, we have some unique skill sets and capabilities at the NIH exactly in the areas that you brought up, and we are absolutely going to have to bring them to bear in this program.

And I think about it from the standpoint of view of investments that are being made and that will be made, and what would draw individuals to invest in a uniform approach. What would bring the value to them? And I think that's exceptionally important because, I'm sorry, NIH cannot pay for all of this. This is just too large, too costly. So you're going to need to have those who are contributing. In a way that would make this project keep going and keep going on a large scale that you are anticipating. Thank you. Thank you, Rhonda. Rafael? Hi, thank you. So, I want to share my main concern about this and about this proposal. It relates to why it's failed so many times in so many institutions.

And it has to do with the difficulty in sharing data, clinical data. There's so many regulations and concerns about privacy and hoarding from investigators that get to write more papers if they don't share their data that I have yet to see any institution succeed. And it's not because of lack of machine learning methods. It's not lack of data for sure. It's just it's lack of the ability to share data. And I don't know if it's the case, but it does seem like. One big driver of that is NIH regulations that, that you know, have this indirect effect of making it hard to share, even within institutions. So, this is particularly concerning here because there's, there's also plenty of stories, examples where some machine learning expert claims, 'Pathologists or radiologists are no longer needed; my method is just better than them.' They get a science paper, but then when they tried in any other hospital, it fails completely.

So, you need to test across hospitals and/ or across, measuring, measuring measurements wherever the measurements are being taken. And just to develop methods that are robust to that, which I don't think are around yet. You have to share data across sites. So, if we can't even share data within sites, How are we going to share data across sites? That does seem to be not a technical or scientific problem. It seems to be completely a political problem. And a lot of it having to do with privacy regulations, which maybe they're necessary, but I don't think we can have both the privacy regulations and the ability to share data as we need to make this succeed. So I'm wondering if there's, it will be some kind of incentive or some kind of procedure to facilitate this hurdle that's been around for 20 years now and has kept people from succeeding at projects like this.

Thank you. Rafael, thank you for raising that. As I see it, you mentioned two concepts. One is testing across hospitals, validation. And I think that's extremely important. That's exactly the premise of what we're trying to address with this validation center to prove that we have generalizability. Your bigger comment was about data sharing and culture and regulations. Totally, totally, totally agree with that. You know, we published an NIH data sharing requirement two years ago, and the community hates it, you know, for exactly the reason that you mentioned that. You know, we've heard every single complaint. And I just wanted to highlight one thing that I believe you heard in the Science of Science thing that, you know, it's our firm belief that, you know, these are the smartest people in the world that we're dealing with.

And if we incentivize people to want to do something, they will want to do it. And, you know, we've really been trying to push this NIH data sharing so-called S-index challenge. You know, can we develop a metric that will go up, you know, if you share more data and it's good? And can we get, can we work with Google Scholar, you know, pick your, you know, different people to really publicize this and get it into promotion in 10 years? I think that's one of the ways that we can help drive culture change to really push this forward, you know, and address the things that you're talking about. So, you know, Rafael, thank you. So I would have a concrete suggestion, which is to make people put their money where their mouth is.

So, you could have a requirement for the funding opportunity that if you can't demonstrate that in your institution, you're not sharing data. Like, if EHR data is just stuck in one place, this one investigator that somehow happened to get their hands on it, then they don't get to participate. I don't know if there's a way to do that, but I think under the institutional metric that we have in grants we might require that they should they demonstrate very clearly that that they are in fact capable of sharing data otherwise you're going to give funding to an institution and then they're just impossible for them to do it they just don't want to do it and you get stuck with and maybe you'll have papers but they won't actually help you succeed Yeah, and maybe I could just jump in.

You know, we'll build, we have some successes in the imaging community, some precedents. So I mentioned the Mid-Dirk Consortium, which is 24 different institutions and three majors. Absolutely. I'm more concerned about EHR. Yeah, okay. Well, that group, actually, it took a couple of years, first to share the imaging data, and now the other, the EHR and clinical data. is beginning to flow. So, you know, it's been a struggle. But I think that as people see the opportunities and the advantages and systems that are structured in a way that can help facilitate it, they'll emulate those, hopefully, as we progress. It also brings up the federated learning approach. And sometimes that's the option to move towards as once you've exhausted your data repositories from a few different sites, and then you want to engage other partners and other sites.

But definitely a big problem. Thank you. Okay, moving to Russell. Great. Thank you both for a phenomenal presentation. This is obviously so important to the future of all of medicine and really appreciate your bringing this forward as an initiative. I want to address a little bit of

Rafael's comments and Kevin's comments, and then I have a question. Kevin's comments with respect to AI Ready and the lessons learned could not agree more. I've had a ringside seat from the concept clearance four years ago, and one of the major programs is based at my university. So I've gotten to see how that has progressed, and it has been remarkable. First of all, the overcoming challenges to creating these datasets was significantly greater than one would have anticipated.

And that did get into interoperability issues, data sharing issues, the trivial things of, you know, memoranda of understanding between organizations to share the data in the first place; and the lack of standardization around those created very large bureaucratic barriers to rapidly deploying, all of which, though, were eventually overcome. And at this point, at least the AI Ready project, which I'm most familiar with, is on track to complete its 4,000-subject multimodal dense data set enrollment on time by the end of the fourth year. In fact, to your point, Raphael, the data sharing is a requirement of that grant. And if you go to AIReady. org, I think it is, you will see the current data set. It's up; you can download it.

And it's well over a thousand subjects with complete datasets that are available for anyone just like all of us or any of the other large datasets. And I think this is something NIH uniquely brings to the field is the ability to require open sharing of data as a requirement for funding. And I think that's very, very powerful here. I also want to address a little bit of the comments about data interoperability. I know Mike has thought about this extensively and actually published a very nice editorial in our literature, which he wrote in collaboration with a lead at the FDA. As well as at the Office of the National Coordinator for Health Information Technology. And that latter group actually exists to drive data harmonization in the clinical sphere.

And I would strongly recommend that they have a seat at the table as you're designing these programs. You know, DICOM is a standard. It's out there. It is voluntary. And as we all know, there are vendors who subscribe to DICOM, and then there are vendors who say they subscribe to DICOM, and then there are vendors who ignore DICOM. If there's going to be IP at the end of this that's going to be useful for prediction, you will need to be in the DICOM space to participate. And I really encourage you to leverage that opportunity to try to bring vendors to finally complying so that their data is interoperable between sites. Finally, the question is, it was unclear from the presentation what the policy is going to be on the IP that arises from this. So you have a very large data set or data sets that come out of this, extremely rich. Presumably, the community will be able to mine this for ideas. What will be the policy in terms of protection of that IP? Because as others have mentioned, there's a huge interest in this in the commercial space. And it would be highly desirable for the work that comes out of this project to be able to make it to the public.

Well, Mike, maybe I can just jump in on the IP issues. We don't see any specific at the beginning, kind of at the outset, in the absence of having seen any proposals come, deviations from you know, our normal IP policies. In fact, you know, we want to continue to encourage IP and commercialization is probably our biggest mechanism of dissemination. But there's also a kind of concurrent movement towards open science and algorithms that are widely distributed

and validated in a community sense. And so, we'll just have to see how our community is responding to this, uh, you know, much of what I do in terms of device development, um, we and I still have a lab, and you know, we do devices, and we we make the raw data from the device available to our entire community.

We publish the algorithms on GitHub; I mean, these are this is a very strong movement within the device and the technology development community. We publish entire bills of materials so people can build the same device or deviations of it. So, this is quite a powerful movement. We don't know exactly where all of this is going to go. We'll see probably a little bit of all of the above. But our main passion is to be able to get this to patients and to be able to move and accelerate what we know are fabulous discoveries and new insights that are happening all across the country. But, patients are still getting, you know, the two-line impression from the radiology report. So I wish I had an upfront answer to all this, but it's going to be an evolving story.

Mike? Yeah, you know, Russ, I would just thank you for your comments, Russ. When the hands started going up, I didn't see yours right away. I wondered if something's wrong. And then I'm glad to hear from you now. No, no, I agree with every single thing. I'm just going to highlight one thing that Bruce did not talk about, which is, Russ, your point about working across agencies and this project that we've worked on with the FDA and with the ONC slash ASTP, the Assistant Secretary for Technology Policy. I would just underscore, Russ, what you said, that in a world where there are sticks and carrots, I think there's a role for each of them. And we viewed this as a carrot.

We tried to come up with rules when the field wasn't moving in a certain direction after about the 15 to 20 years that I've been involved with it. What can we do in terms of sticks to move that? And those were the ones that we created. And so totally agree that we could do some stuff with them involving interoperability and really appreciate your raising that. Great. Okay. Thank you. Our last council member with our hand raised is Jean. Please go ahead. Okay, this is going to be quick, I hope. I am really excited about this project. Obviously, I do imaging, I do AI, the combination is amazing. And I'm so excited about the possibilities. You have funded Retro Repro Men by David Kennedy, who actually did a lot of this work in terms of building tools for the interoperability.

And I think obviously, it's NIH-funded by you. I'm thinking a lot of those tools could be used here. I wanted to go back to what Linda said; um, it's sometimes really difficult in imaging-it depends on what machine the strength of the machine whether or not it's a particular kind of scanner, what kind of scanning you did-there's a lot of work there to bring those pieces together. I totally believe that the integration would lead to innovation and huge impacts. So I'm in. I just think a lot of what we're saying is there's a lot of work here, probably more than we think about right now. That cannot stop us. But I think when I saw you had mostly money towards going from the data to the clinic, I think that may take more work than we think.

And I would really want to put a lot of it into the integration. integration part. Once we're doing good integration and we have the algorithms to really help us, especially with prediction, I'm really excited about prediction. It's how we could use AI to predict who will or will not get a particular disease. i feel there's a lot there so i it could blow up science in terms of what we think about it i think it's going to change and transform this whole ecosystem but the integration part i feel there's going to be probably more resources more things we need to do and to encourage integration across different sites having a coordinating system um site

which i'm not sure i saw you had in there but how we'll bring all that data together so everyone will be learning at the same time from each other as opposed to rebuilding the wheel over and over thank you very much gene yeah i think we're both in i guess what we say violent agreement about that um and you know that's part of i think the brilliance of our Our colleagues who, who sort of structured all of these elements to fund and the overall plan, which spends an enormous amount of time and resources making sure that the algorithms are thoughtfully developed and validated, and then can potentially piggyback onto ongoing studies, these ancillary studies that are happening everywhere, you know, from ECOG-ACRIN, which is sort of the big beast at the NIH.

to industry-sponsored drug trials where they may have longitudinal imaging for patients. But again, no one really looks at the images. They just say a very brief impression of a few kilobytes or kilobits. And so we're hoping the community really just takes advantage of those things, the enormous ongoing effort and the enormous resources that we're going to put in. Uh, in addition to the funding but the expertise that all of us have developed over the last several years to to really bring people together and to accelerate the commercialization and the translation of these approaches. Thank you. I'd also just like to highlight that Carolyn has put several comments in the chat about having existing MOUs with FDA to specifically get early feedback from the agency.

So, I think that's an example with respect to sort of the regulatory piece where we are able to learn from existing programs, but also with the data sharing requirements, having those considerations be built into the NOFO and have those the award selection and funding be specifically tied to those requirements as well. So definitely really, really appreciate all of the feedback that's being provided here. And that will be, you know, if this concept is approved, you know, that will absolutely be integrated into how the NOFOs are written and how the program is structured. Okay, I think that closes the discussion here. Francesca, I'll turn it over to you. Then that brings us to the last vote for today; we're going to call for a vote on before we vote, sorry I was trying to unmute.

Can you clarify a little bit more about that last comment? Um, what are we we're voting for? The concept to be approved and then is the the funding then guaranteed or is that or is there a next discussion about it? Well, let me try to explain how that normally works. If a concept is approved, then that gives us the go-ahead to move forward if funding is available, if the circumstances are correct, and if everybody is ready to do it. That does not guarantee that it goes forward. Of course, an important part is the entire discussion that we heard today. Program

staff will take all those comments into consideration and build those in, which then has an influence on what your question was. You know, what will the budget be?

Well, if we build much a bigger castle, then, of course, the costs will be much higher and we need more money to do so, whereas you understand what I'm trying to say. So did that answer your question, Rafael? Absolutely. Yeah. Excellent. OK, so with that, then I'm going to call for a motion, a motion for approval of the Common Fund concept clearance entitled Precision Medicine with AI Integrating Imaging with Multimodal Data Prime AI Program. Is there such a motion? I see so moved. I see second. Any additional discussion at this point? I see no hands. I see no chat info. We are doing hopefully the last time our hand raising votes. Christina, please go ahead. Thank you, Dr. Greeter. As a reminder, only council members should participate. This is a vote on the motion for approval of the proposed OSC concept clearance. Please raise your hand now to vote aye.

Thank you. I see 12 hands voting aye. Please lower your hands.

Please lower your hands. One more. Thank you. All right. Next, please raise your hand to vote nay.

Thank you. I see two hands. Please go ahead and lower those hands. Thank you so much. Up next, please raise your hand to vote abstention.

Not seeing any hands, this concludes the vote. The motion as stated has passed. Thank you, Christina. Back to you. Thank you all very much. So this concludes the concept clearance portions of our agenda. So now I want to pivot. Dr. Johnson, did you want to say something? Yeah, hi. I just realized, are we going to have a chance to discuss DSI Africa? That was on our slate. Did that just get tabled or what happened with that? That is currently tabled, so it is not on the agenda for this month's meeting. It is under consideration still for the May council meeting. Okay, great. Okay. Okay. So the next thing we want to address quickly, I know we're over time, and I appreciate all of you spending a few extra minutes with us.

But we want to have some reflections from our departing council members. So I want to take a moment to extend my sincere gratitude, but really on behalf of all of DPC and all of NIH to our departing members. So your thoughtful guidance has really played a vital role in helping NIH navigate complex health challenges and advance scientific discovery. really, truly fortunate to have such a dedicated group of leaders helping to shape the future of biomedical and behavioral research. So once again, thank you so much for your service, your expertise, and your unwavering commitment to the NIH mission. So we want to ensure that our departing council members have the opportunity to share their insights and leave us with some parting wisdom if they so choose.

So please feel free to come off mute to share your thoughts. I know that one of our departing members, Kristen Ardley, had to jump off already. But if Linda or Kevin or Rhonda or Susan or Anna Maria would like to say a few words, we would welcome that feedback. Kevin, please go

ahead. Thank you. Um, I had some prepared remarks I thought I would say them so as I step down from this remarkable committee, I want to take a moment to reflect not just on our shared work but on the principles that have anchored my career in my service here. I believe deeply in the scientific process not as a rigid protocol but as a dynamic engine for truth driven by curiosity, discipline, skepticism and creativity; and I've come to appreciate more than ever that meaningful innovation emerges when people, process, and technology are aligned with intention.

It's from that vantage point that I feel compelled to express some concerns about the pace and direction of recent changes at the NIH, often framed as progress. Progress is essential, but it is not synonymous with speed. People remain at the heart of science. Our trainees, who depend on stable mentorship structures, are communities who deserve clear, trustworthy science communication. Our policymakers who rely on evidence to inform both global and national health decisions, our fellow scientists whose work is enriched through deliberation and collaboration, not disruption, and U. S. citizens whose health is the linchpin of a vibrant nation. Likewise, process matters. New initiatives, no matter how promising, require thoughtful implementation strategies, inclusive engagement, and iterative feedback loops. It's easy to pilot as we talked about earlier; it's much harder to sustain.

The success of NIH programs will hinge not just on vision, but on scaffolding that preserves institutional memory and rewards learning along the way. And technology, while exciting and my thing, must be approached with a commitment to validation. Whether we're talking about AI, mHealth, novel diagnostics, these tools are only as good as the data that shapes them and the rigor with which they are tested. Innovation without verification can unintentionally widen disparities or erode public trust. So, to my fellow council members, thank you. You are not only among the most preeminent scholars in your respective fields, you're generous, thoughtful, and collegial in ways that have made every meeting for me feel like a master class in both science and citizenship. It's been an honor to work alongside you.

And to the incredible NIH staff who support our work behind the scenes, You are the unsung backbone of this enterprise. Thank you for your tireless coordination, your attention to detail, and your grace under pressure. You are the catalyst of the NIH's mission to create new knowledge. You make the work possible and, frankly, better. So, I leave this committee with gratitude, conviction, and hope, and with a commitment to keep championing the values that have always moved science forward, people, process, innovation, and technology in harmony. Thank you. Thank you so much, Kevin. Rhonda, please go ahead. Thank you. I want to iterate or repeat many things that Kevin has already said, particularly in terms of the excellent support that we received from the staff at NIH, but also more importantly, the collegial relationship with those who are on the Council of Council.

Not being a researcher or in academic medicine, but in what I would call more healthcare delivery, you have given me the opportunity to learn so much in terms of not only science, innovation, and new ideas, but also understanding the complexity and the complications in terms of trying to bring those scientific ideas forward. So I thank you for that. It has allowed me to become humbled to the complexity and the difficulty in bringing things forward. A lot of my

early work in the field had to do with crossing the Quidichasm. I was on that committee. And so, I hold very dear the issue of it taking 17 years to take a scientific fact and get it into delivery into the system. And so, that's one of the things that's highly motivated me.

And I will say that many of the things that I've heard here over the years, over the 12 years I've been involved, not only from the mental health perspective, but from the general medical perspective, have encouraged me that NIH is trying to close that gap and trying to close the number of years that it takes to do this. With that being said, I would say that there are some things that I think NIH, being in the position that you have, particularly being under the guides of Congress and others, that you have the connection to be able to navigate the regulatory waters. And I think it was mentioned by one of the last speakers, be able to use that in order to bring the field to move together and to begin to engage in terms of commitment.

I think the one thing that we really don't want is to create, particularly in this world of new innovations, a fragmentation that cause more problems in the long run. And I'll just cite electronic medical records is one of the major ones, is an example from the very beginning that became privatized, but certainly created a bunch of fragmentation and costs on the parts of health system. So, the major things I want to say is that science is absolutely significant and essential. But it has to be trusted science. As I've mentioned earlier today, being able to communicate the science not only to those who can directly use it beyond the ways that are being done right now, so a wide dissemination and acknowledgement, but also to the public and being able to explain to the public in a way that it can be digested.

I would also suggest that private sector be involved in terms of helping you to shape what are the areas that are most important. From the private sector perspective, there are many pain points that are out there that can be helped by attention from NIH, particularly in terms of furthering research, but more importantly, bringing that research into the real world so that there's immediate learnings that can occur, not only in terms of the data that's collected and analysis, but also in terms in terms of directly to providers who are engaged in this as well as the patients. I would also say the area that I think is really important is the governance. And that, I would say, you're very good at pulling together all your divisions and also pulling in many governmental entities.

But I think in order to really further what you're doing and bringing it to the real world with adoption and implementation. Need to, again, bring in other stakeholders. I would cite one of the areas that is really important in terms of innovation and moving things forward besides the research and the funding that you bring forward would be funding that comes from other organizations. Alignment around those organizations, consolidating or focusing their funding, their philanthropic funding, will bring more power to the system to be able to make changes in order to accommodate the research that you've given. So with that, with my 12 years being here, again, I'm very grateful for the opportunity. I've learned a lot. I'm sure there's more to be learned, and I will continue to follow you on the web.

But I really want to say that it's been a fabulous opportunity, and thank you so much. Thank you so much, Rhonda. Linda, please go ahead. Yeah, I just also want to thank, express my gratitude for-I felt very honored to have been part of this committee and to be on the council. Although I served on like the NIDA council and the BSC on NIDA in the past, I think being on this committee, this council really gave me a much broader perspective of how NIH functions. And so it's really been a tremendous learning experience for me. So I'm very grateful for that. The six years seem to have passed like a blink of an eye. And it seemed like I think we kind of missed out a little bit because of COVID, that we didn't have as many in-person meetings.

We've had very few in-person meetings as a result of that. And I think having the in-person meeting really does add value to the communication between the members and the discussion. I definitely felt that, especially early on during the pandemic, when we started doing all this virtual meeting; everything is just, you know, it was very matter-of-fact. You know, everyone just reports and the discussion just wasn't as engaging as they were had we been in an in-person setting. So that's my only feedback about that. Otherwise, I want to thank the KIPC program, the staff, everybody. I've had a wonderful experience. Thank you. Thank you so much, Linda. Okay. I'm not seeing any other hands raised. I will note that Susan put her comments in the chat.

So I will just close by saying, you know, I am incredibly grateful both on behalf of Deepa Kepsi and NIH, but for myself personally, because this has been an extraordinarily helpful experience as I learn more about Deepa Kepsi. And I just really appreciate all of the thoughtful input and critical discussion and constructive feedback that was provided today. And I'm really looking forward to getting to know all of you better. And I hope that many of the Council members who are rotating off will still continue to remain engaged through our working groups. I think we already had some expressions of commitment earlier in the day from some of those folks, so that's fantastic. I am delighted to inform you all that the next Council of Councils meeting will be in-person, and it is scheduled for May 29th and 30th, so we really look forward to seeing you next month. Francesca, anything else? No? Okay. Where did my gavel go? Oh, okay. There. The council meeting is adjourned. Thank you. Thank you all. Thank you. Bye, everybody. Bye. Thanks, Francesca. You're amazing. Well, thank you for saying that, especially with my boss here. She is amazing. Yeah. See you later. Bye, Kevin. all right.