88th Meeting of the National Cancer Institute (NCI)
Council of Research Advocates (NCRA)
National Institutes of Health (NIH)

NIH Campus
March 1, 2023

Members Present

Ms. Belinda Bachini
Mr. Yelak Biru
Dr. Victoria Buenger
Ms. Melissa Buffalo
Mr. Marty Chakoian
Ms. Annie Ellis, *Chair*
Mr. Nathaniel Ferre
Ms. Joya Delgado Harris
Dr. Brittany McKelvey
Mr. Robert Riter
Ms. Kristen Santiago
Mr. Kevin Stemberger
Dr. Nicole Willmarth

Speakers

Dr. Monica Bertagnolli, Director, NCI

Dr. James Doroshow, Deputy Director, Clinical and Translational Research, and Director, Division of Cancer Treatment and Diagnosis (DCTD), NCI

Dr. Yvonne Evrard, Operations and Program Manager, Patient-Derived Models Repository (PDMR), NCI

Ms. Holly Gibbons, Deputy Director, Office of Government and Congressional Relations, NCI

Dr. Arunan Skandarajah, Presidential Innovation Fellow, Advanced Research Projects Agency for Health (ARPA-H)

Ms. Amy Williams, Acting Director, Office of Advocacy Relations (OAR); Executive Secretary, NCRA, NCI

Guests

Dr. David Bowen, Senior Advisor, ARPA-H

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Welcome and Opening Remarks

Ms. Amy Williams and Ms. Annie Ellis

Ms. Williams opened the meeting at 10:00 a.m., welcomed Council members and attendees, provided brief opening remarks, and reviewed the day's agenda.

Ms. Ellis called the meeting to order, reviewed the conflict-of-interest rules, read the public comment statement, and confirmed that a quorum of members was present. She invited NCRA members to briefly introduce themselves.

NCI Director's Update

Dr. Monica M. Bertagnolli

Dr. Bertagnolli began by noting it is an honor to be NCI Director and to work with NCRA members.

Recent Progress

President Biden continues to show unwavering support for NCI efforts. In the February 7 State of the Union Address, President Biden indicated that he intends to go big to achieve goals that are worthy of comparison to the effort that got humans to the moon in 1969. He called on all to work to end cancer as we know it, cut the cancer mortality rate by 50 percent in 25 years, turn more cancers from death sentences into treatable diseases, make life better for people living with and surviving cancer, and provide more support for patients and families.

The White House released a list of significant achievements on the one year anniversary of the reignited Cancer Moonshot, including establishing nearly 30 new federal programs, policies, and resources; closing the screening gap; tackling environmental exposures; decreasing preventable cancers; advancing cutting-edge research; supporting patients and caregivers; and generating new actions and collaborations from 60 private companies, academic institutions, nonprofit organizations, and patient groups.

Dr. Bertagnolli emphasized that with President Biden's support, now is the time to take significant steps to end cancer as we know it.

NCI Appropriations and Budget Outlook

On December 29, 2022, President Biden signed legislation that provides funds to NCI, NIH, and other federal agencies through September 2023. Congress increased NCI's budget by $408 million in Fiscal Year (FY) 2023, which is a $386 million increase from the base budget and a $22 million increase to the final year of initial Cancer Moonshot funding through the 21st Century Cures Act.

The increase to base funding allows NCI to fund more compelling investigator-initiated cancer research and continue to support key research outside the research project grant (RPG) pool (e.g., Clinical Trials Network, core support for NCI).

- RPG funding allows investigators across the nation and world to transform their innovative ideas into answers that drive progress. The payline dictates the number of grants the NCI budget can support. With the increased funding in FY2023, NCI increased the payline for R01 grants for established and new investigators to the 12th percentile and for R01 grants for early-stage investigators to the 17th percentile. These payline increases fund a larger number of grants.
- FY2023 funding also was allocated to critical infrastructure needs, such as information technology, that will expand data sharing across the research community, amplify cancer research

results, drive new collaborations, and ensure maximal use of prior research investments.

These funding decisions required a 2 percent reduction of the payline for noncompeting grants and payline reductions for NCI's Divisions, Offices, and Centers. These decisions reaffirm NCI's commitment to distribute federal funding broadly. Increases in the payline are a commitment to sustaining funded grants for at least 5 years (out-year costs) and require increases in out-years budgets to sustain funding at the current percentage level. NCI is hopeful and looks forward to supporting the President's budget when it is announced. Dr. Bertagnolli noted Ms. Holly Gibbons, who would be presenting later in the day, would share more about appropriations and the budget outlook.

Dr. Bertagnolli also mentioned the recent publication of two NCI Bottom Line blogs titled *NCI Funds More Research Grants Thanks to Action by Congress*, in which she wrote about NCI funding decisions and challenges, and *Doing More—Together—to End Cancer as We Know It*.

National Cancer Plan

As the leader of the National Cancer Program, NCI has assembled a new National Cancer Plan that outlines the goals, strategies, and actions required to reduce cancer mortality and dramatically improve the lives of all people affected by cancer. The National Cancer Plan embraces the idea that everyone has a role to play and illustrates how people contribute to progress and the many interrelated actions needed to end cancer as we know it. NCI currently is obtaining input from stakeholders and the plan soon will be presented for final approval.

Budget Proposal

Dr. Bertagnolli presented the Professional Judgment Budget (PJB) proposal for FY2024, which was included in NCI's annual report. NCI requested a substantial investment to advance cancer biology, prevention, detection and diagnosis, treatment, and public health and cancer control research and training and infrastructure. The proposed budget also will be used on data, data collection, and the dramatic expansion of NCI's National Clinical Trials Network.

Program Updates

Dr. Bertagnolli announced the launching of the new Clinical Trials Innovation Unit (CTIU)—a collaboration between NCI, the U.S. Food and Drug Administration (FDA), and the extramural cancer research community—that will select high-priority studies for new study designs and operational procedures and speed clinical testing to deliver new approaches for diagnosis, treatment, and prevention of cancer.

On Friday, March 24, the Childhood Cancer Data Initiative (CCDI) will hold its annual symposium to describe CCDI's progress and opportunities for 2023 and beyond. Dr. Bertagnolli emphasized that this is a unique community that has been galvanized by the need to learn from every child with cancer and understand every facet of the child's life and disease to make progress. This effort demonstrates the power of data sharing and collaboration and is the goal paradigm.

Discussion

- Ms. Ellis expressed excitement about the National Cancer Plan and thanked Dr. Bertagnolli for efforts in that area. She also expressed excitement about the new CTIU and noted that, as advocates, NCRA members are interested in patients everywhere. She asked what the plans are to ensure that those innovations are scalable to all patients. Dr. Bertagnolli responded that the "patients everywhere" issue is foundational, and success is dependent on addressing it on multiple

fronts, which includes designing accessible, welcoming, and engaging clinical trials and ensuring that clinical trial structures are reviewed by cancer centers.

- Ms. Ellis noted that institutions are having staff retention issues. She asked what the effect of the two percent payline reduction on researchers might be, whether NCI is having staff retention issues, and how advocates might be able to help. Dr. Bertagnolli replied that payline cuts are one of the current big challenges and noted that there is intense concern about whether postdoctoral fellows and trainees are adequately supported. The question is whether NCI funds more grants or funds fewer grants more adequately. The answer to this challenge is not simple, but NCI aims to find the best approach to support the best science.
- Dr. Buenger thanked Dr. Bertagnolli for highlighting CCDI. She encouraged NCRA members to attend the CCDI annual symposium because this initiative is a good pilot project for issues that are of concern to advocates, including data sharing, molecular characterization, longitudinal data collection, and the need for federated systems. Dr. Bertagnolli explained that CCDI's success is due to commitment across the community, assembling around a common purpose, and adequate funding. Assembling data systems and ensuring access to data are not trivial; this requires an enormous amount of work, planning, and support, but the benefits are incredible. This is the infrastructure that is needed to make progress.
- Mr. Biru expressed appreciation for Dr. Bertagnolli noting that funding by itself is not enough to reach goals. Innovative collaboration and all of society are also needed to move forward. Advocates, nonprofit organizations, and others are ready to help NCI. He also thanked Dr. Bertagnolli for sharing her personal journey and challenges. This gives voice to the voiceless and shows that one can live and work through cancer. Dr. Bertagnolli thanked Mr. Biru and shared that the community of people with cancer provided her with strength in the past as a physician and now as a cancer patient.
- Mr. Chakoian commented that he is grateful for federal government funding of prostate cancer research. He noted that much of that research is done outside NCI and asked what NCI can do to ensure that the research across federal agencies is coordinated and that duplication is avoided. Dr. Bertagnolli agreed and noted that NCI cannot act alone. The National Cancer Plan is an all-of-society plan and is being discussed across multiple agencies.
- Mr. Ferre expressed appreciation for the renewed Cancer Moonshot beginning to make connections instead of remaining an isolated initiative because a large component of this research is ensuring that the general public is aware of this work. He asked whether there are any public messaging strategies to accelerate public awareness. Dr. Bertagnolli responded that the National Cancer Plan will help ensure the general public understands its role in contributing to the president's goal of ending cancer as we know it.
- Dr. McKelvey asked about NCI's focus and intentions for long-term survivorship research. Dr. Bertagnolli replied that NCI has a dedicated program in survivorship research.

NCI's Clinical Trials Program

Dr. James H. Doroshow

Dr. Doroshow reported on the initial and continuing effects of the COVID-19 pandemic on cancer clinical trials, NCI's 2023 strategic vision for clinical trials, and activities to ameliorate current clinical research workforce issues.

COVID-19-Related and Ongoing Barriers to Clinical Trial Accrual

From the start of the pandemic, NCI confronted multiple challenges, including the need to conduct in-person study activities virtually (e.g., informed consent, visits to receive investigational study drugs, and assessments of patient safety and study adherence) and managing limited access to cancer care personnel/facilities due to reprogramming of clinical research resources for care of COVID-19 patients.

There are critical shortages of staff (e.g., research nurses, essential healthcare workers) and institutional central research services (e.g., institutional review board services), which have significantly diminished trial availability and accrual for all populations, including underserved populations, and have led to substantive delays in reporting of results.

NCI's clinical trials program responded to these issues by shifting to electronic consenting, providing oral investigational agents directly to patients, initiating electronic study audits, facilitating the use of telemedicine, limiting the impact of minor study deviations on trial conduct/evaluation, implementing decentralized testing, and developing and implementing a new strategic plan for NCI's clinical trial programs.

Dr. Doroshow shared monthly accrual data of national, investigator-initiated, externally peer-reviewed trials for 2020–2022 and numbers of annual enrollment to national, investigator-initiated, externally peer-reviewed, and pharmaceutical trials for 2019–2022. The data showed a significant accrual decrease at the beginning of the COVID-19 pandemic. These data also show that, unlike national trials, accrual to investigator-initiated and externally peer-reviewed trials has not recovered.

About a year and a half ago, the Science Technology Policy Institute administered an NCI Cancer Center Clinical Trials Workforce survey to assess the ongoing impact of the COVID-19 pandemic on clinical trials. Responses showed a decrease in accrual, mainly due to limited research staff capacity, which resulted in prevention of trial opening and forced accrual holds, and recruiting of staff by institutions, the pharmaceutical industry, and contract research organizations that offer opportunities with higher pay or career advancement.

NCI's 2023 Vision for Clinical Trials

In the midst of the COVID-19 pandemic, the NCI Clinical Trials and Translational Research Advisory Committee Strategic Planning Working Group (SPWG) reassessed the strategic vision for the clinical trials system for 2030 and beyond. The result of this work was a set of 15 recommendations and 3 operational initiatives.

The goal of the NCI strategic vision for clinical trials for 2023 and beyond is to develop flexible, faster, simpler, less expensive, high-impact clinical trials that seamlessly integrate with clinical practice. This will be accomplished by:

- Streamlining processes for trial design and execution
- Focusing on essential endpoints
- Decreasing regulatory hurdles and broadening trial access
- Increasing efficiency of data collection.

Dr. Doroshow described the work around streamlining clinical trials and 1 of the 15 SPWG recommendations: limiting clinical trial data collection in late-phase trials to essential data elements. The NCI-convened *ad hoc* Streamlining Clinical Trials Working Group reviewed the NCI Coordinating

Center for Clinical Trials' analysis of recent phase III treatment protocols and advised on ways to optimize data collection.

The Working Group's recommendation and proposed standard practices apply initially to a subset of trials (e.g., phase III and phase II/III, Investigational New Drug [IND]-exempt trials). The proposed standards focus on adverse events, medical history, concomitant medications, physical exam, laboratory tests, imaging and other assessment procedures, and patient-reported data. The Working Group identified several candidate low-value data categories. The goal is timely implementation of standard practices for data collected in a subset of trials (e.g., NCI phase III and phase II/III adult, IND-exempt trials), which are expected to reduce operational burden and provide insights that will inform development of data collection standards for other types of trials.

In addition, the S2302 Project Pragmatica study is an upcoming IND prospective randomized study of ramucirumab plus pembrolizumab versus the standard care for participants previously treated with immunotherapy for stage IV or recurrent non-small cell lung cancer in standard practice. This study will implement minimal data collection (e.g., the only adverse event collected will be hospitalization of patients) and could change the standard of care for patients with non-small cell lung cancer.

Addressing Critical Clinical Trial Workforce Issues

Dr. Doroshow outlined the multiple approaches being used to address workforce issues, including streamlining/standardizing trial activation processes and increasing flexibility for remote work. NCI also is considering developing a new training grant program that will support development of careers in clinical trials and is conducting a Virtual Clinical Trials Office pilot study.

Discussion

- Ms. Ellis thanked Dr. Doroshow for addressing the state of clinical trials office personnel and describing the steps being taken to alleviate workforce issues. She asked whether patient advocates were part of the Working Group that developed the clinical trial streamlining recommendations. Dr. Doroshow confirmed that there were patient advocates in the Working Group.
- Ms. Ellis noted that low-value adverse events sometimes are underreported and are significant in cases where there are modest improvements in survival. Dr. Doroshow responded that life-altering adverse events (e.g., chronic adverse events) will be collected whereas non-life-altering events, such as blood count abnormalities that are of no value, will not.
- Dr. Willmarth pointed out that reducing the collection of unnecessary data also will decrease the burden on patients and their caregivers. Dr. Doroshow replied that, as a patient himself, he understands that reducing the frequency between computerized tomography (CT) scan imaging has a big impact emotionally and financially. It is not clear whether the "standard" protocols that have been implemented to date have an impact on whether or not trials will meet endpoints; thus, the question of which data are necessary to meet endpoints is being carefully considered.
- Mr. Biru asked whether staff shortages are affecting predominantly underserved communities and, consequently, the diversity of clinical trials, and what NCI and FDA can do to assure clinical trial inclusivity. Dr. Doroshow responded that staff shortages have affected all populations, including minority populations. He described how the Virtual Clinical Trials Office pilot study was modeled on the virtual approach implemented by the Louisiana State University's NCI Community Oncology Research Program (NCORP). The NCORP site recruited staff to work

remotely and acquired direct access to practices' electronic health records, which resulted in a rapid accrual increase during the pandemic. The Virtual Clinical Trials Office pilot study will test whether this approach works at the national level with a small number of NCORP and academic sites. The success of this pilot study may facilitate provision of services to rural and underserved sites.

- Mr. Ferre asked whether NCI is planning to pilot the Virtual Clinical Trials Office study on a large scale and about its timeline. This study will be done on a large scale (six to ten sites). The personnel recruitment process is active. NCI cancer center directors have been queried about interest in participating in this study, and the response has been overwhelming. Groups will be prioritized based on level of need and whether minority population accrual will be facilitated. This pilot aims to enhance NCI trials, not pharmaceutical industry trials.
- Dr. Buenger asked about opportunities to continue using telemedicine approaches and how advocates can help. Dr. Doroshow replied that the optimal ways to conduct clinical research using telemedicine are not yet clear. NCI funding of additional research on how to optimize these activities would be beneficial. He encouraged NCRA members, in their role as advocates, to help incorporate telemedicine use into standard of practice for writing trial protocols.

Budget and Legislative Report

Ms. Holly Gibbons

Ms. Gibbons presented an overview of leadership changes in the 118th Congress, debt limit and ongoing budget negotiations, FY2024 appropriations, and recent congressional briefings.

Leadership Changes

In the House, Republicans now have the majority, with Kevin McCarthy serving as Speaker; Steve Scalise, as the majority leader; and Tom Emmer, as majority whip. Hakeem Jeffries is the new minority leader and Katherine Clark is the new minority whip. In the Senate, Chuck Schumer now is serving as majority leader and Mitch McConnell as minority leader. Dick Durbin is the majority whip and John Thune is the minority whip. With the retirement of Patrick Leahy, Patty Murray has become President Pro Tempore.

The House Committee on Energy and Commerce (E&C) and Health Subcommittee also have seen leadership shifts. Cathy McMorris Rodgers is Chair and Frank Pallone is the ranking member of the E&C Committee. In the Health Subcommittee, Brett Guthrie is Chair and Anna Eshoo is the ranking member. In the Senate Committee on Health, Education, Labor, and Pensions, Bernie Sanders is Chair and Bill Cassidy is the ranking member.

For the first time, Chairs and ranking members of both the House and Senate Appropriations Subcommittees are all women (Susan Collins, Patty Murray, Kate Grainger, and Rosa DeLauro), as is the Director of the Office of Management and Budget (OMB; Shalanda Young). Rosa DeLauro also serves as the ranking member of the Labor, Health and Human Services (L-HHS) Subcommittee alongside the new Chair, Robert Aderholt. In the Senate, Tammy Baldwin is the new L-HHS Subcommittee Chair and Shelley Moore Capito is the new L-HHS ranking member.

Debt Limit Negotiations

The timing for the debt limit negotiations is running directly in parallel to the appropriations process and the end of the current fiscal year. An agreement between the administration and House Republicans is

necessary to raise the debt limit. House Republicans are proposing significant spending cuts and calling for a return to FY2022 funding levels; however, there is no intention to cut the defense budget. This could lead to an 18 percent cut for nondefense discretionary spending, which includes NIH and NCI.

FY2024 Appropriations

Independent of the debt limit negotiations, it is speculated that a full-year continuing resolution (CR) with funding at FY2023 levels is possible. If Congress cannot agree for FY2024, a series of CRs or a full-year CR are possible.

For FY2023, there were increases to funding for NIH, NCI, and ARPA-H. The President's budget will be released on March 9 and initiate the appropriations process. The NCI PJB is released several months prior to the President's budget proposal and is transmitted directly to the President and Congress to provide information about cancer research opportunities.

Upon release of the President's budget, the congressional appropriations committees likely will begin hosting hearings with the OMB Director, Cabinet Secretaries, and U.S. Department of Health and Human Services (HHS) operating division leadership. These hearings rarely conclude at the start of the next fiscal year; therefore, a CR at the start of FY2024 would not be surprising.

Recent Congressional Briefings

Ms. Gibbons closed by listing recent congressional briefings in which NCI colleagues participated, including the National Cancer Prevention Workshop hosted by the Less Cancer Foundation, the Littlest Tumor Foundations' Annual Neurofibromatosis Briefing, and the American Association for the Study of Liver Diseases' Combatting Liver Disease Congressional Briefing.

NCI Patient-Derived Models Repository

Dr. Yvonne A. Evrard

The NCI Patient-Derived Models Repository is a national repository of patient-derived models (PDMs) that serves as a resource for academic discovery efforts and public-private partnerships for drug discovery. The PDMR develops a wide range of PDMs representing different stages of cancer for a variety of cancer types from residual tumor tissue provided by clinics and researchers. The PDMR also accepts models developed in other laboratories.

Development and Use of Patient-Derived Models

Models of cancer are developed within the DCTD Biological Testing Branch (BTB) by implanting patient tumor tissue into host mice to generate patient-derived xenografts (PDXs), organoids (PDOrg), and cell lines (PDC). Once the PDX tumor successfully grows in the host mouse, the tumor is used for multiple research purposes, including implantation into additional host mice to make more tumor for future use, storage for future distribution to researchers, pathology assessment, molecular profiling, and implantation into host mice to be used for preclinical drug testing. The PDMR delinks and deidentifies tumor tissue and does not report follow-up data back to clinicians, allowing the development of several models without restricting oversight.

These models of cancer undergo extensive quality control and are fully characterized before being distributed to researchers around the world. The PDMR obtains information (e.g., clinical history) from the original patient and clinicians and performs a pathology assessment (e.g., histology) to ensure that the developed model matches the original tumor; conducts molecular profiling to identify key mutations; and

collects model growth data. A publicly accessible database houses this information for researchers to select models that best fit their research goals.

Not all tumor cells grow in the laboratory setting. The PDMR calculates each cancer type's "take rate" to focus on receiving more tissue from cancers with lower "take rates" and increase the possibility of developing those models for researchers. Colon adenocarcinoma is one cancer type that grows well in the laboratory environment with a "take rate" of 70 percent. Prostate cancer tumors have proven difficult to grow in the laboratory; this cancer type has a 3 percent "take rate." The PDMR is continually trying to improve the development of these models to make them available for research.

Investigators from academic institutions, nonprofit organizations, industry/commercial groups, and government/intramural entities around the world request and use PDMR models to conduct studies. Examples of research projects that use these models include:

- Basic research studies to investigate basic biology of oncogenesis, mechanisms for resistance to therapies, metastasis, and optimization of cell culture media
- Biomarker research and discovery studies to identify models with specific mutations that may predict a response to targeted agents or combinations of agents, biomarkers associated with a specific disease type or whose expression changes with treatment, and protein complexes in diseases to provide evidence for treatments
- Therapeutic research and discovery studies to find translatable strategies that may benefit patients with specific mutations and agents that could be moved forward to a PDX study to support a future early-phase clinical trial.

For example, PDMR PDX models of rare cancer have been used by DCTD BTB to identify novel therapeutic combinations that inhibit tumor growth more than the individual single agents and move them forward to early-phase clinical trials.

Advocacy Groups and Individuals Involved with the NCI PDMR

One key goal is to find champions to share models or provide tumor tissue samples for future model development to help a broader group of researchers. Dr. Evrard highlighted that the development of models—including the reestablishment of models from a depositing laboratory, expansion, and full characterization—is a years-long effort and requires continuous communication.

The PDMR has multiple active and developing collaborations. For instance, a physician working with the Cholangiocarcinoma Foundation deposited 10 cholangiocarcinoma cell lines to the PDMR in 2021; PDX models are being developed. Surgeons at Johns Hopkins University and Ohio State University have shared rare sinonasal cancer cell lines for development of models for research. The PDMR also is actively collaborating with a physician at Johns Hopkins University who deposited a pediatric low-grade glioma cell line and a team of transplant surgeons at the University of Pittsburgh Medical Center that has deposited pediatric hepatoblastoma tissue. Active discussions with the Lobular Breast Cancer Alliance and Fight Colorectal Cancer are ongoing.

Ways to Interact with NCI PDMR

Avenues to interact with the PDMR include connecting with laboratory scientists who have developed models to make those models available to a broader community and connecting with clinicians who can provide residual tissue from medically indicated procedures for model development. NCI takes on the burden of the cost of expanding and distributing the developed models.

Discussion

- Ms. Ellis thanked Dr. Evrard for the presentation and expressed excitement about PDMR's work and these models being made available to researchers. She asked whether the PDMR is receiving specimens from diverse populations. Dr. Evrard replied that there is low (10 percent or less) representation of minority groups in available models. To increase this number, the PDMR is working with minority underrepresented NCORP sites and a consortium that has models from ethnic and racial minority populations. The PDMR's efforts to increase the diversity of models are continuous and involve constant communication and outreach.
- Ms. Ellis asked about the number of PDX models derived with primary and metastatic cancer samples from the same patient and their usefulness. Of the 650 publicly available PDX models, 15–20 matched sets of pancreatic cancer models have been developed with postmortem tissue. The PDMR also has developed a small number of matched models using longitudinally collected tissue from NCI clinics.
- Dr. Willmarth asked whether the PDMR collaborates with both NIH/NCI grantees and nongrantees and about the application process. Dr. Evrard explained that although the majority of groups the PDMR works with are funded by NCI, the PDMR collaborates with both NIH/NCI grantees and nongrantees. The application process involves contacting PDMR; obtaining informed consent—a barrier in this process; providing patient information; and shipping tissue on the day of surgery. The PDMR does provide funding for some of these activities. Dr. Willmarth expressed interest in discussing glioma models with Dr. Evrard.
- Dr. Buenger commented that lack of awareness about partial funding support of activities by the PDMR and clinical teams' resources (e.g., personnel to prepare and ship tissue to PDMR) seem to be barriers to obtaining samples. She asked what the barriers to development of models are once cell lines are deposited. Dr. Evrard responded that insufficient staff and the slow-moving model development processes are barriers. Some cancers grow faster than others in tissue culture. Dr. Evrard noted that tissue samples are processed immediately for implantation into the host mouse or development of PDCs upon receipt.
- Mr. Biru asked whether models and cell lines are available for blood cancers. Dr. Evrard noted that key malignancies are currently being characterized, and a pipeline to process these samples is being developed. The PDMR is collaborating with the NCI Histologic Oncology Group and clinical sites, which will provide samples of different blood cancers, including acute myeloid leukemia and myeloma.
- Mr. Biru also asked what the oldest cell line is. Dr. Evrard explained that the PDMR's goal is to keep material as close to the patient as possible; therefore, cell lines are kept young by banking them at early passages.
- Ms. Santiago asked if it would be possible to report information back to patients. Dr. Evrard reiterated that none of the PDMR's activities are Clinical Laboratory Improvement Amendments-certified; thus, all samples are delinked and deidentified, and no information can be reported back to patients. PDMR activities were designed to freely conduct large-scale research without the administrative burden of reporting information to clinicians.
- Mr. Chakoian commented that few medically indicated procedures would allow collection of bone metastasis samples from patients and asked if samples are regularly obtained from the rapid autopsy program. The PDMR obtains bone metastasis samples collected during removal of limbs

and bone marrow aspiration and currently works with four rapid autopsy programs. A postmortem procedure yields 8–12 different pieces of tissue—including bone metastases—from unique sites from patients who have consented.

- Mr. Riter commented that the PDMR obtains samples from industry partners. Dr. Evrard clarified that industry/commercial groups (pharma groups) can request models from the PDMR but do not provide samples. These groups sign a Material Transfer Agreement, which limits the use of these models to internal research purposes.
- Ms. Ellis asked whether there are efforts to increase the "take rate" of prostate cancer models. Dr. Evrard noted that there are many researchers around the world who are developing prostate cancer models. The PDMR has obtained a few of these models and is attempting to partner with many of these groups to increase the availability of these types of models, which would be beneficial because this type of cancer is common.
- Dr. Buenger asked Dr. Evrard to characterize the cooperative attitude across institutions regarding the sharing of tissue and whether institutions would choose to send samples to the PDMR rather than use the tissue. Dr. Evrard said that both cases likely are true. The clinical groups with which the PDMR collaborates prioritize how the sample is divided based on the patient and end use to ensure that each group is obtaining the best tissue for their research purposes.
- Dr. Buenger shared that at a recent International Society for Biological and Environmental Repositories conference, she observed a cooperative attitude in the pediatric community but not in groups that collect tissue samples from adults. Dr. Evrard indicated that the attitude towards sharing of tissues is specific to different groups. The groups that work with the PDMR collaborate well. Many groups recognize gaps in cancer models and are attempting to connect and find ways to generate more models. Dr. Buenger commented that this should be encouraged.
- Mr. Stemberger noted that many of the groups that work with the PDMR have historically generated their own models. It is important for biorepositories to not be redundant and allow for collaboration. He has observed that this collaboration has improved over the past few years and appreciates seeing this collaboration at the NCI level. Dr. Evrard agreed that many groups that request models from the PDRM also have models at their own sites and use the PDMR to fill gaps. In developing the PDMR, NCI's original goal was to ensure that this repository was not in competition with other existing repositories. In its current phase, the PDMR is expanding to have encompassing representation.

Status of ARPA-H

Dr. Arunan Skandarajah

ARPA-H is a federal research and development funding agency that is an independent component of HHS within NIH. To advance quickly, ARPA-H will build upon the infrastructure that organizations like NCI have already established. ARPA-H's Director, Dr. Renee Wegrzyn, reports directly to the HHS Secretary.

Congress has provided $2.5 billion, none of which is allocated to specific disease areas. ARPA-H will not have internal research labs or be grant based; instead, cooperative agreement, contract, and other transaction authority mechanisms will be used to drive toward specific outcomes and shift resources as needed. ARPA-H's structure facilitates the execution of high-risk, high-impact research.

The ARPA-H health ecosystem is designed to be complementary to healthcare agency systems and comprises customers (the public, healthcare providers, patient groups), performers (academia, industry),

and stakeholders (FDA, NIH Institutes and Centers, Centers for Medicare and Medicaid Services, Health Resources and Services Administration, nonprofit organizations).

Core Components and Organizational Attributes

Programs led by Program Managers (PMs)—science- and management-trained individuals who are expected to launch a program every year through their 3-year tenure—are a core component of ARPA-H. Programs are two to four years long and consist of multiple performers—academic researchers, small companies, medical research institutions—who carry out different projects. This allows the ARPA-H portfolio to be dynamic and a reflection of the PMs.

Dr. Skandarajah described the organizational attributes of ARPA-H:

- PMs are the nucleus of the organization. A leadership team is built around them.
- ARPA-H seeks to address major challenges, not incremental research.
- PMs are autonomous and will bring in their own big ideas. Once PMs are selected, they will engage with the community by attending forums such as NCRA meetings to obtain input on challenges and metrics.
- PM term limits (renewable once for an additional 3 years) allow inflow of new ideas, create a sense of urgency, avoid building a longstanding entity within ARPA-H, and remove incentives for empires, organization-building, span of control, and bureaucracy.

The ARPA Model

Each PM will identify a difficult health-related challenge that is not easily solvable through traditional activities. The program will be launched and the PM will oversee several groups of performers that compete or collaborate to solve the challenge. Selection of PMs will be done using the ARPA-(H)eilmeier Questionnaire framework, which consists of 10 questions that investigate various aspects of the proposed problem, including the health problem of interest, limitations of current approaches, cost, the proposed approach, and impact.

The life cycle of programs consists of designing well-defined problems in health with stakeholder insights, building a performer team, executing the program and measuring progress against metrics, learning and growth, and commercialization and transition. Success is defined as developing solutions that survive in the wild, removing barriers of today's technologies and systems, and delivering better health to everyone.

Initial mission focus areas of include:

1. Health science futures—expanding what is technically possible, accelerating advances across research areas, and removing limitations.
2. Scalable solutions—addressing health challenges to create programs that result in impactful, timely, and equitable solutions.
3. Proactive health—creating preventative programs to anticipate threats to Americans' health.
4. Resilient systems—building integrated healthcare systems to weather crises.

The Project Accelerator Transition Innovation Office ensures that solutions developed by ARPA-H programs can "survive in the wild" by providing various tailored services at different stages of the program life cycle.

Seeking Program Managers

ARPA-H is actively looking for potential PMs and asking organizations such as NCRA to help identify those individuals. Potential PMs may be at different career stages and should think like a CEO—they must consider aspects such as marketing, research, and implementation. Other traits of potential PMs include having recognized expertise, a serious drive, no fear of failure, curiosity, a customer-centric mindset, and being decisive. ARPA-H is seeking PMs diverse in geography, demographics, experience, and topics. Potential PMs can expect a competitive salary and business and technical team support.

Recent ARPA-H Milestones

Upon onboarding in the first quarter of 2023, the first PMs will begin engaging with communities such as NCRA, and the first programs will launch in during the second and third quarters of the year. ARPA-H currently is engaging with members of Congress, staff, and intragovernmental partners (e.g., NIH, NCI, FDA); university personnel (e.g., Johns Hopkins University, Stanford University, Howard University); and advocacy organizations and professional associations across the U.S. (e.g., Friends of Cancer Research, American Cancer Society). Dr. Skandarajah noted that ARPA-H has met, and plans to meet, with a number of cancer-related organizations.

Cancer Moonshot

ARPA-H may contribute to the Cancer Moonshot by appointing a Cancer Moonshot Champion to identify internal efforts across mission offices, engage stakeholders such as NCRA members on behalf of the government, and collaborate with Cancer Moonshot leaders. ARPA-H PMs can leverage infrastructure of implementation pathways, translate ongoing research efforts into capabilities for researchers or patients, and solve problems prioritized in the Cancer Moonshot that can't be solved otherwise.

Dr. Skandarajah shared examples of notional programs that may address Cancer Moonshot strategic priorities, including the development of digital histopathology capabilities by designing and developing novel multi-omic histopathology assays, using artificial intelligence and machine learning, and bringing data integration into care pathways and digital advocacy.

Discussion

- Ms. Ellis thanked Dr. Skandarajah for the comprehensive presentation and expressed excitement about ARPA-H supporting high-impact research instead of incremental advances.
- Dr. Willmarth asked whether new PMs bring in their own programs in addition to continuing established projects. Dr. Skandarajah noted that as in the models of the Defense Advanced Research Projects Agency and Advanced Research Projects Agency-Energy, PMs are expected to take on programs that relate closely to their technical expertise. People will not be hired specifically to take on programs. Dr. Bowen, senior advisor at ARPA-H, noted that the management of programs may be similar to a relay race.
- Dr. Buenger asked whether ARPA-H incorporates convergent and divergent thinkers into PM and performer roles. Dr. Skandarajah noted that both types of thinkers likely will be hired and highlighted that programs have divergence and convergence elements. For example, PMs will converge to a single solution after groups of performers compete to solve a specific challenge, and Mission Office Directors will check that solutions are relevant to patients.
- Dr. Willmarth asked if there is an opportunity for programs that have failed to continue outside of

ARPA-H. Dr. Skandarajah replied that programs that are not the right fit for ARPA-H may transition to be funded by partners.

- Ms. Ellis commented that since the conception of ARPA-H, there have been many questions about the transition of projects, which seems to vary depending on the project. Dr. Skandarajah explained that those transitions are a metric and ARPA-H will keep revising until those transitions are made. This can be accomplished through different pathways and at different stages (e.g., milestones). ARPA-H will bring alongside potential transition partners that may have funding capabilities for the researcher or implementation. Dr. Bowen added that ARPA-H does not use "success" or "failure" language because in ARPA-H's innovative model, there are different potential paths; all of those—including the "failures"— provide useful information.
- Ms. Delgado Harris asked how ARPA-H is working with the cancer-related organizations that were included in his presentation. Dr. Skandarajah clarified that those organizations are groups that ARPA-H is interacting with and that represent different verticals for ongoing engagement. Hopefully, ARPA-H will engage with many more groups. Dr. Bowen added that it is important that all ARPA-H activities are informed by the patient and provider communities. These organizations may be a source of PMs, promote the agency, and ensure that ARPA-H's activities are grounded by the understanding of the considerations for different groups.
- Regarding the ARPA-(H)eilmeier framework, Ms. Ellis asked if consumers would weigh in on specific projects and whether ARPA-H has an advocacy advisory group. Dr. Skandarajah responded that feedback from patients will be obtained during the program design stage; the first engagement will be through subject matter experts. Ms. Ellis commented that she hopes ARPA-H considers people with lived experience subject matter experts. Dr. Skandarajah agreed and noted that lived experience is important for the formulation of programs and the interim (evaluation) checkpoints. Ms. Ellis noted that advocates appreciate being part of the process.
- Ms. Delgado Harris asked if the ARPA-(H)eilmeier questions are listed in order of importance and whether question nine (To ensure equitable access for all people, how will cost, accessibility, and user experience be addressed?) could be moved up to encourage people to consider health equity. Dr. Skandarajah responded that all questions are evaluated as a set and are not listed in order of importance.
- Mr. Biru asked whether ARPA-H will create a failure repository as a way to learn from the research. Dr. Skandarajah replied that failure will be captured by sharing lessons learned and the barriers that are stymieing progress. ARPA-H is open to program ideas that may address how to capture and communicate failure.
- Mr. Stemberger asked about the transparency of ARPA-H projects and the PM role. Dr. Skandarajah shared that for recruitment, ARPA-H is engaging groups and established experts in different fields and using social media. Dr. Bowen asked NCRA members for recommendations on events, people, and groups with which to engage to gain an understanding of current concerns and provided his contact information. Dr. Buenger clarified Dr. Stemberger's question, which was whether the PM's work at ARPA-H is secret. Dr. Skandarajah replied that while other ARPA's are more secretive by design, ARPA-H's success is about transition and including stakeholders and, thus, is geared toward publicizing the potential funding opportunity and the PMs. PMs are the face of their programs, and this is an opportunity for them to explore new areas and be seen as thought and community leaders.

Certification

I hereby certify that foregoing minutes are accurate and complete.

July 5, 2023 \s\
Date
Annie Ellis
Chair
NCI Council of Research Advocates

July 5, 2023 \s\
Date
Amy Williams
Executive Secretary
NCI Council of Research Advocates