DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH
NATIONAL CANCER INSTITUTE

7th Virtual Meeting of the BOARD OF SCIENTIFIC ADVISORS

Summary of .Meeting

21 March 2023

Virtual Meeting
National Cancer Institute
National Institutes of Health
Bethesda, Maryland

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH
NATIONAL CANCER INSTITUTE

BOARD OF SCIENTIFIC ADVISORS

SUMMARY OF MEETING
21 March 2023

The Board of Scientific Advisors (BSA), National Cancer Institute (NCI), convened for its 7th virtual meeting on Tuesday, 21 March 2023, at 1:00 p.m. Dr. Keith T. Flaherty, Director of Clinical Research, Massachusetts General Hospital Cancer Center, Professor of Medicine, Harvard Medical School, presided as Chair. The meeting was open to the public on Tuesday, 21 March 2023, from 1:00 p.m. until 4:52 p.m. for the consideration of new requests for applications (RFAs), Cooperative Agreements (Coop. Agr.), and requests for proposals (RFPs) of new and re-issue concepts presented by NCI Program staff.

BSA Board Members Present

Dr. Keith T. Flaherty (Chair)
Dr. Chandrakanth Are
Dr. Karen M. Basen-Engquist
Dr. Otis W. Brawley
Dr. Andrew T. Chan
Dr. Nelson J. Chao
Dr. Gloria D. Coronado
Dr. Mark P. Doescher
Dr. Chyke A. Doubeni
Dr. Shelton Earp
Dr. Jennifer R. Grandis
Dr. Dorothy K. Hatsukami
Dr. Trey Ideker
Dr. Karen E. Knudsen
Dr. Michelle M. Le Beau
Dr. Ana Maria Lopez
Dr. Karen M. Mustian
Dr. Raymond U. Osarogiagbon
Dr. Sylvia Katina Plevritis
Dr. Erle S. Robertson
Dr. Robert D. Schreiber
Dr. David Sidransky
Dr. Cornelia M. Ulrich
Dr. Samuel L. Volchenboum
Dr. Robert H. Vonderheide
Dr. Richard C. Zellars

Board Members Absent

Mr. Timothy Babich*
Dr. Suzanne J. Baker
Dr. Lisa A. Newman*
Dr. W. Kimryn Rathmell

Others Present: Members of NCI's Scientific Program Leadership Committee, NCI staff, members of the extramural community, and press representatives.

*Pending appointment

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I. CALL TO ORDER AND OPENING REMARKS— DR. KEITH T. FLAHERTY

Dr. Flaherty called to order the 7th virtual meeting of the Board of Scientific Advisors (BSA or Board) and welcomed current members of the Board, National Institutes of Health (NIH) and National Cancer Institute (NCI) staff, guests, and members of the public. Dr. Flaherty reminded the Board members of the conflict-of-interest guidelines and confidentiality requirements. Members of the public were invited to submit to Dr. Paulette S. Gray, Director, Division of Extramural Activities (DEA), in writing and within 10 days, comments regarding items discussed during the meeting.

Dr. Flaherty called Board members' attention to future meeting dates listed on the agenda, noting that the 2025 dates will need to be confirmed.

Motion. A motion to approve the 2025 BSA meeting dates was approved unanimously.

Dr. Flaherty noted that the next BSA meeting will be a joint meeting with the National Cancer Advisory Board (NCAB), scheduled for 14–15 June 2023, and will be held in person with remote participation available.

II. NCI DIRECTOR'S REPORT—DR. MONICA M. BERTAGNOLLI

Dr. Monica M. Bertagnolli, Director, NCI, welcomed BSA members and attendees to the 7th virtual meeting of the BSA and provided an update on recent cancer research progress and what it will take to sustain and accelerate it. She provided the NCI budget outlook, a status of the National Cancer Plan, and program and research updates.

Recent Cancer Research Progress: Sustaining and Accelerating. Dr. Bertagnolli noted that President Joseph R. Biden continues to convey strong support for cancer research and reiterates his intent to "go big" and aim high to achieve bold goals for progress against cancer. During his February 2023 State of the Union Address, President Biden called attention to Ava Barron, a 3-year-old girl who has a rare kidney cancer, who (along with her parents, Maurice and Kandice) was in the audience. Dr. Bertagnolli commented that the struggle they have experienced was evident on the parents' faces, as well as their courage and hope. The great news is that Ava's outlook is very promising and is a reminder that that the NCI is here to serve people like Ava and her family.

With the reignited Cancer Moonshot℠, President Biden emphasized working together to end cancer as we know it and announced loftier goals of a 50 percent reduction in cancer mortality in 25 years. The aims are to change more cancers from death sentences into treatable diseases and provide more support for patients and families. Achieving this goal will transform the experience of those with cancer. The NCI soon will release an analysis conducted in the Division of Cancer Epidemiology and Genetics (DCEG) on what it will take to achieve the President's 50 percent goal; the analysis will be published in *Cancer Discovery*, with an accompanying commentary. The NCI also will host sessions during the 2023 American Association for Cancer Research annual meeting on this topic.

NCI Budget Outlook. Dr. Bertagnolli reported that the President's fiscal year (FY) 2024 budget was released on 9 March 2023 and included a total budget of $7.8 billion (B) for the NCI, which would be a 6.9 percent increase above the FY 2023 enacted budget. She reminded the BSA members that the 21st Century Cures Act funding is in its final year and has provided the Cancer Moonshot funding, which has launched a wide array of transformative research projects. The President's budget is proposing $216 million (M), which matches the FY 2023 enacted budget and proposes a $500 M increase for FY 2024, totaling $716 M in increases for the NCI. This budget also proposes reauthorization of the

21st Century Cures Act and mandatory funding of $1.45 B budget authority for the NCI in FY 2025 and FY 2026. In recent years, the appropriations from Congress have been higher than the President's proposed budget, signifying their steady commitment to cancer research progress. With this budget request, however, President Biden has strongly communicated to Congress his intent to aim high. Dr. Bertagnolli noted that Ms. M.K. Holohan, Director, Office of Government and Congressional Relations (OGCR), NCI, will provide further details on the NCI FY 2024 budget and political landscape later in the meeting.

Dr. Bertagnolli highlighted that NCI received good news from Congress in December 2022. President Biden signed legislation that provided funding to the NIH and other federal agencies through 30 September 2023, and the NCI received a $386 M increase to its base budget; $22 M is allotted for the final year of the initial Cancer Moonshot funding, for a total of $216 M for those investments. She commented that this base increase makes it possible to fund more compelling investigator-initiated cancer research and continue to support key research efforts outside of the Research Project Grant (RPG) pool. These include the clinical trials networks, NCI-Designated Cancer Centers (Cancer Centers), and training.

In 2023, with implementation of the RPG funding policy for FY 2023, the NCI increased the R01 payline to the 12th percentile for established and new investigators for competing grants, which continues an upward trend since FY 2019, and to the 17th percentile for early stage investigators (ESIs). With these increases, the NCI was able to fund more than 100 additional R01s and ESI awards than in the previous year. RPG funding allows investigators across the nation to transform their innovative ideas into answers that drive progress for cancer patients. In addition, funding critical infrastructure, including information technology (IT), is a major priority for the NCI. These infrastructure components amplify research results, drive new collaborations, and ensure maximal use of NCI's prior investments in research. Thus, the NCI also allocated new funding to meet these goals. Dr. Bertagnolli noted that, as a result of the decisions to support the RPG pool and critical infrastructure, the NCI needed to cut costs elsewhere. The noncompeting grants (years 2–5) are continuing at the 98 percent level. The NCI also has reduced its spending considerably. Once increased baseline costs were allocated, the NCI implemented a 2 percent across-the-board reduction in funding for NCI Divisions, Offices, and Centers.

Dr. Bertagnolli noted the challenges that factor into making the decision to increase paylines. Because of the out-year costs incurred by each increase, funding in the subsequent years needs to increase to accommodate funded grants and maintain the payline. She emphasized that the R01 payline of 12th percentile is the highest since FY 2010. She discussed these budget decisions in a recent post in the *NCI Bottom Line: A Blog About Grants and More*. She also posted in *Cancer Currents: An NCI Cancer Research Blog* about the opportunity for cancer research, highlighting progress from decades of investment, President Biden's commitment, and important new NCI programs. Dr. Bertagnolli underscored the importance of the "last mile," from validation of a successful intervention against cancer to its widespread adoption and broad implementation. Completing this last mile requires participation from many others throughout our society. She emphasized that ending cancer as we know it and ensuring that all advances benefit everyone who needs them will take an all-of-society approach to bridge the gap. She also noted that the NCI cannot achieve this goal alone.

National Cancer Plan. Dr. Bertagnolli explained that the NCI has worked closely with researchers within and outside the NCI to produce a new National Cancer Plan to align broad societal engagement and focus on critical needs to end cancer as we know it. The Plan emphasizes achieving goals to allow people to live free from the harmful effects of cancer, meaning everybody with cancer and every type of cancer. The Plan embraces the idea that everyone has a role to play across federal agencies, as well as throughout industry, academia, advocacy groups, and nonprofits and among caregivers and individual patients. The intent is that any organization or person who reviews this Plan will see where they fit and can contribute to progress. The Plan provides a framework that will help everyone understand the full

range of what is necessary to be able to strategize and work together to sustain and accelerate progress. The final phases are currently in progress and include receiving input from a wide range of stakeholders. The Plan soon will be finalized and communicated widely to the public.

The National Cancer Plan is aligned with, but is not the same as, the reignited Cancer Moonshot; they are complementary. The Plan provides a vision for everyone across all of society to work toward those goals and focuses on how to utilize the collective resources to achieve the fastest possible results to end cancer as we know it for all people. The Cancer Moonshot is how the President engages the cancer research community to mobilize society to take action and bring government agencies together to focus and work together, and the President is advocating for the resources needed to accelerate progress. The NCI is coordinating with the White House Office of Science and Technology Policy (OSTP) to ensure that the Plan provides a focus for achieving the goals of the Cancer Moonshot to address the question: What must we accomplish to achieve the broad goal of helping people with cancer live full and active lives free from the harmful effects of cancer?

Building on the NCI's initial charge of leading the National Cancer Program as part of the National Cancer Act (NCA) of 1971, a new National Cancer Plan is being assembled that outlines the goals that must be achieved to reduce cancer mortality and improve the lives of people affected by cancer. The Plan will incorporate a multifaceted approach that recognizes that the NCI alone cannot achieve the goal of reducing the cancer mortality rate by 50 percent during the next 25 years. The National Cancer Plan will include roles for the NCI, as well as other federal agencies, private industry, academic institutions, nonprofit organizations, advocacy groups, and patients and their caregivers. The Plan defines specific areas of focus that will engage both NCI's intramural and extramural research teams and expected contributions by the Frederick National Laboratory for Cancer Research (FNLCR) to be discussed in future meetings. After review by the NCAB, the Plan will be communicated to the public through the NCI's website and social media platforms, news outlets, and public events.

Program and Research Updates. Dr. Bertagnolli updated the BSA members on NCI program and research activities. The recently established Advanced Research Projects Agency for Health (ARPA-H) is an important new partner for cancer research. Dr. Bertagnolli explained that she has been in regular contact with Dr. Renee Wegrzyn, ARPA-H Director, to decide how ARPA-H and NCI can have the most powerful collaboration. Several ideas from across the NIH have been received and forwarded to Dr. Wegrzyn. The NCI and ARPA-H are complementary, with notable differences in their operations. The NCI often requires, and has for many decades, taking the long view and sustaining its programs over time. The NCI is responsible for cancer research from fundamental science to care delivery research to ensure that a laboratory discovery translates into a clinically tested procedure, drug, or device that benefits people. The ARPA-H focus is similar to that of a rapid deployment team that identifies key issues that are amenable to a high-risk, high-reward research focus. ARPA-H then engages the most important players from across the research and development ecosystem to help solve such problems in a relatively short time frame. The NCI views itself as the recipient of these solutions that ARPA-H will be able to offer and as the one providing scientific leadership to projects so that they best address the needs of cancer research.

The highly successful Cancer Grand Challenges collaboration has entered into a new phase. On 8 March 2023, the NCI, in partnership with Cancer Research United Kingdom (UK), announced nine new research challenges aimed at addressing profound problems in cancer research. The list can be accessed from either the Cancer Grand Challenges website or the NCI website. International teams are invited to submit their approaches to address these challenges by 22 June 2023. In FY 2024, up to four winning teams will be awarded $25 M each over 5 years to complete their research. The NCI–Cancer Research UK partnership underscores the NCI's commitment to support the brightest minds across the global research community as they tackle some of the most complex challenges in cancer research.

NCI clinical trials are essential to turning research outcomes and those possibilities into treatment, prevention, and early detection or diagnosis methods. For several reasons, not enough people are participating in NCI clinical trials, especially those from minority groups or from rural areas; furthermore, trial results are not disseminated rapidly. New structures that are more nimble and more inclusive of all the people served are needed. To address these concerns, the NCI launched a Clinical Trials Innovation Unit (or Unit) to spearhead progress. This Unit is a collaboration among the NCI, the U.S. Food and Drug Administration (FDA), and the extramural cancer clinical research community. The Unit will select a number of high-priority scientific questions that are amenable to radically new study designs and operational procedures in a non-incremental process. The Unit will engage the partners necessary to break the mold and form a more effective new path to results. She emphasized that this new Unit encompasses aspects of clinical trials to engage potential participants more broadly and deliver results faster. These include study eligibility, comparator arms, endpoints, diagnostics, telehealth, data collection procedures, and participant engagement strategies. The NCI anticipated that successful approaches developed and piloted by this Unit will then transition to become mainstream.

Dr. Bertagnolli highlighted three recent examples of notable extramural research advances. First, research has demonstrated that early detection of cancers can significantly improve outcomes. Unfortunately, not enough people are getting the recommended cancer screening. A new NCI-funded study found that among a sample of private-sector workers, mammography and colorectal cancer screening were higher in areas where workers had paid sick leave mandates. These findings suggest that a lack of paid sick leave coverage presents a barrier to cancer screening and could inform potential policy solutions that could boost screening and save lives. Second, studies have shown that drinking alcohol can increase the risk of several types of cancer. A Division of Cancer Control and Population Sciences (DCCPS)–funded study revealed that most Americans were not aware of this connection. The study concluded that numerous changes need to be made to raise public awareness of this fact. Because awareness does not guarantee action, further research will be necessary to solve these challenges. Third, researchers may be on the path to new answers for Ewing sarcoma, an aggressive childhood cancer that also occurs in some adults and is particularly difficult to treat.. Research sponsored by the Cancer Moonshot Fusion Oncoproteins in Childhood Cancers Consortium found that the ETV6 protein modulates the fusion oncoprotein responsible for the majority of Ewing sarcomas. The hope is that this insight can be used to develop a targeted drug that interferes with the action between ETV6 and the fusion oncoprotein and can lead to an effective treatment.

The Childhood Cancer Data Initiative (CCDI) is progressing and meeting expectations in aligning data to improve understanding of childhood cancers. These data have been challenging and costly to obtain. The NCI is making great strides to provide much-needed childhood cancer data to scientists conducting this research via the CCDI. This focused program has made significant progress in accumulating data that have been historically difficult for researchers to access and for research teams to share. Dr. Gregory Reaman, Scientific Director, CCDI, brings his vast experience from his time leading the Children's Oncology Group and working at the FDA. On 24 March 2023, the CCDI leadership will host its annual symposium to convene experts from across the country to discuss overall progress. The NCI is excited to highlight new resources that are available to the scientific community, as well as highlight future opportunities. Attendance will be either in person or virtually, and anyone interested in childhood cancer is encouraged to participate. The aim is to understand how to scale this initiative to all of NCI's efforts and as a plan for the future. CCDI is demonstrating the great power of data sharing and collaboration, and the NCI anticipates that this initiative will become a paradigm for what can be done for everyone with cancer and every research team.

In closing, Dr. Bertagnolli noted that several activities are in progress, extending from step-by-step science to high-level planning to aligning the cancer research enterprise. The NCI is seeking all of society to achieve the progress everyone is expecting.

In the discussion, the following points were made:

- In the new Clinical Trials Innovation Unit, all aspects of clinical trials are open to innovation and will be explored, including adopting more structured forms of authoring trials to streamline downstream data analytics and bioinformatics and performing implementation science on the research.

- The first innovation of the Unit was the launch of the S2302 Pragmatica-Lung clinical trial, which is a registration trial designed to be nimble, simple, and straightforward. This trial engages numerous communities across the United States through the National Clinical Trials Network (NCTN) and NCI Community Oncology Research Program (NCORP). Having the FDA involved in the initial and ongoing discussions has been a powerful force to ensure that these trials can be conducted.

- ARPA-H has an Open-Office Broad Agency Announcement to which the scientific community can submit proposals and ideas for projects. The ARPA-H leadership is rapidly hiring project managers to commence work. Dr. Dinah S. Singer, Deputy Director, Science Strategy and Development, NCI, is coordinating interactions between the NCI and ARPA-H. The NCI will be the end user of any products developed and will serve as a test environment.

- The NCI is working with OSTP on what the reissuance of the NCA would entail; further details will be forthcoming. The President has clearly conveyed that the NCI has the tools and authority necessary for making the fastest possible progress in cancer. The whole-of-government approach will continue regarding NCA reissuance and is included in the Plan, which also has been presented to the U.S. Department of Health and Human Services (HHS).

- The NCI is open to a mechanism to increase salaries for cancer research trainees, with a solution that benefits all parties. This topic will be discussed with the Cancer Center directors during their May 2023 retreat, as well as with NCI's advisors during the June 2023 Joint BSA/NCAB meeting. Increasing the award amounts of grants will result in fewer grants funded and subsequently, a decrease in paylines. One goal of the National Cancer Plan will be to optimize the workforce, but no mandates to increase salaries have been introduced.

- The purpose of the Unit, within the context of its whole-of-government approach, is to simplify clinical trials and meet the needs of diverse communities in the United States, including minority groups and those located in rural areas who desperately need access to lifesaving therapies. Each community will need a different solution and will require engaging different groups of individuals, which is a theme interwoven in the National Cancer Plan.

- In terms of research in the Unit, NCTN leadership can propose and receive ideas from the scientific community. In addition, ideas can be submitted to the Unit's co-directors, Dr. Sheila Prindiville, Director, Coordinating Center for Clinical Trials (CCCT), NCI, and Dr. Michael J. Morris, Medical Oncologist, Memorial Sloan Kettering Cancer Center. The NCI anticipates activating three or four studies in the Unit this first year, and those will not be observational studies. The priorities of NCORP and the NCTN are different, and two preliminary general ideas on symptom intervention and data collection might fit with NCORP activities.

III. THE NCI RESEARCH PROJECT GRANTS (RPG) BUDGET AND BEYOND—DR. DOUGLAS R. LOWY

Dr. Douglas R. Lowy, Principal Deputy Director, NCI, presented the distribution of the appropriated NCI FY 2023 budget, RPG pool trends over the past decade, and RPG considerations, with a focus on FY 2023. He expressed appreciation to several NCI staff for their support generating these data: Ms. Kiara Montavon, NCI Office of Budget and Finance; Ms. Vivian Pham and Ms. Denise Brandenburg, Office of Extramural Finance and Information Analysis; Dr. Christine Burgess, Center for Research Strategy; and Ms. Kelli Marciel, Office of Communications and Public Liaison.

NCI FY 2023 Budget Appropriations. Extramural funding comprises three-quarters (74 percent) of the NCI overall budget, with the remainder dedicated to other funding, which includes research and management support and intramural research. The RPG pool is the largest investment of NCI funding, at 44 percent of the total budget. Non-RPG activities include the Cancer Centers, Specialized Programs of Research Excellence (SPOREs), and training. From FY 2018 to FY 2022, the NCI appropriation increased to $1.07 B; 53 percent ($550 M) supported the RPG pool and 47 percent supported other investments. Over this 4-year period, the RPG pool budget was increased from 41 percent to 44 percent, representing an average of $140 M annually, and it is anticipated to increase further in FY 2023.

RPG Pool Trends. The rate of applications and number of applicants seeking support from the NCI increased substantially faster than the rates in other NIH Institutes and Centers (ICs). From FY 2013 to FY 2022, the number of NCI applicants increased by approximately 45 percent as compared to about 20 percent in the other NIH ICs. From FY 2001 to FY 2022, the number of applications and applicants to the NCI substantially increased, and the success rates decreased. Although these rates have increased over the past few years, those increases have not reached the level of the NIH as a whole, partly attributed to non-RPG research.

From FY 2016 to FY 2022, the NCI increased the paylines for ESI R01/R37 applications from the 12th to 16th percentile, and the number of funded awards increased from 84 to 133. For established investigators, the payline was at the 10th percentile in FY 2016, decreased to the 8th percentile in FY 2019, returned to the 11th percentile in FY 2021, and then remained stable. During this period, the number of awards funded increased from 650 to 805.

RPG Considerations—FY 2023. Dr. Lowy briefly reviewed the RPG funding policy for FY 2023 previously discussed by Dr. Bertagnolli and noted that R21 grants will be funded at the 9th percentile. He reminded BSA members of the two overall funding categories within the RPG pool: Competing (new) awards and noncompeting (out-year) awards. To prioritize funding, the NCI generally funds only the first year that awards are made. Almost all RPG awards are multiyear awards, with an average duration of 5 years.

There are two main sources of dollars available for the funding for competing and noncompeting RPG awards. These include the turnover of funds from the completion of noncompeting RPG awards in the prior year and the addition of funds from the NCI appropriation, if turnover dollars are insufficient. The dollars derived from completed awards are usually lower than what is needed. Three main factors account for this discrepancy: (1) the number of completed awards will be smaller than the number of new competing awards; (2) inflation, where the average cost of each competing award will be higher than average cost of each completed award; and (3) out-year costs of multiyear awards. Because of all these considerations, the NCI increases its annual investment in the RPG pool.

Dr. Lowy described the option of funding noncompeting RPG awards at less than the 100 percent of commitment level. The NCI considers this option only when funds from the turnover of completed awards plus funds from NCI appropriation are insufficient. In these situations, the overall issue is whether

to prioritize making more awards (i.e., having a higher payline) or to prioritize funding noncompeting grants at 100 percent. The NCI typically prioritizes funding additional competing awards and has consulted with the BSA and NCAB about these decisions, which seem to reflect the sense of the cancer research community.

Dr. Lowy noted some investment considerations. At the end of FY 2022, the total RPG pool investment was $2.9 B. The R01/R37 grants made up approximately 61 percent of the total RPG pool. Each 1 percentile increase or decrease to the new/competing grants payline adds or subtracts $33 M, and similar changes to the noncompeting grants add or subtract $21 M. These various considerations led the NCI to arrive at the current funding decisions. Dr. Lowy indicated that the NCI has prioritized RPG funding, adding $550 M during FY 2018 and FY 2022; a similar amount is projected for FY 2023. A considerable amount of extramural research funded by the NCI is outside the RPG pool. To that end, the NCI has not neglected the other parts of its research portfolio.

In the discussion, the following points were made:

- The number of applications the NCI receives has been stable over the past few fiscal years compared with the numbers received by the other ICs, which have slightly increased.

- To increase the opportunities for ESIs to make an impact with their first R01 award, the NCI instituted the R37 (Method to Extend Research in Time, or MERIT) Award and policy. The R37 provides a 2 year extension of funding after the initial 5 years of funding. However, the 2 year extension is not automatic.. Eligible ESIs write a progress report; the NCAB reviews the report and makes a determination with input from the NCI program managers. The majority of ESIs in this category have had outstanding progress and have continued their research with the additional 2 years of funding.

- The statistics of the NCI investments associated with increasing or decreasing paylines by 1 percentile ($33 M for competing awards and $22 M for noncompeting awards) are striking and have been underappreciated in the cancer research community. Distinguishing between outstanding applications not funded at the 12th and/or 15th percentile remains a challenge for the NCI.

- The increase in NCI funding success rates across all grants over the years, narrowing the gap with the other ICs, is very positive.

IV. LEGISLATIVE REPORT—MS. M.K. HOLOHAN

Ms. Holohan reported on the debt limit and budget negotiations, the FY 2024 President's budget request, the appropriations process, and oversight in this 118th Congress. Debt limit increases are routine (20 have been passed since 2001) and have been passed in both Republican- and Democratic-led administrations. The urgency of a debt limit and the impending date to consider extraordinary measures (so called X-Date) is that it serves as leverage for budget decisions. In fact, a debt limit increase has been part of the calculations for most of the large budget deals seen in the modern history of Congress, the most recent being the Budget Control Act of 2011, which set spending caps for 10 years. This year, the debt limit urgency coincides with the House governing party (i.e., Republican party) pledge to return to FY 2022 funding levels and to have budget reduction planning linked to a debt limit suspension vote. Several other conditions are involved in this process and, understandably, many members of Congress have been concerned about receiving large omnibus bills just prior to the vote without adequate time to review them. Another challenge will be advancing 12 bills through each subcommittee separately, which will take some time.

The President's FY 2024 budget was released later than normal, on 9 March 2023, and prioritizes investments in clean energy, climate science, and new technologies. This budget proposes a 3.2 percent increase for defense funding. In returning to the FY 2022 levels, the funding would be roughly an 8 percent decrease below the FY 2023 enacted budget. After removing defense funding and programs, which will not be reduced, the decrease to all other nondefense discretionary spending will be 22 percent. In this budget request, the President proposes a unity agenda among portions that could have bipartisan support, such as the reignited Cancer Moonshot's goals and mental health investments. Ms. Holohan echoed Dr. Bertagnolli on the proposed increases to the NCI and discretionary funding and clarified that the 21st Century Cures Act reauthorization could include a specific section for the NCA and other related biomedical research. For the NIH, the overall increase is 1 percent, and for ARPA-H, the budget proposes $1 B. The President's budget also highlighted examples of Cancer Moonshot–related proposals, which emphasize the whole-of-government approach to ending cancer. Aside from the NCI, proposed increases include $20 M to the Health Resources and Services Administration, $108 M to the Indian Health Service, $70 M for military and environmental exposures research, $15 M to the Centers for Disease Control and Prevention (CDC), and $50 M to the FDA Oncology Center of Excellence. In addition, this budget also includes a new mandatory proposal for a national program to eliminate hepatitis C, which is a major risk factor for liver cancer.

Ms. Holohan reminded the BSA members that the President's budget begins the NIH/NCI appropriation process. Congress has the constitutional power of the purse and decides appropriations. Considerations to the budget are typical, regardless the status of the majorities in Congress or what the Executive Branch proposes. Regardless, the mixed reception in the press, new approaches, and focus on cancer research are positive. Even when the President and the majority in both chambers of Congress are the same party, Congress rarely appropriates exactly what the President requests. Appropriators tend to be a less partisan group. The current leaders of the House Appropriations Committee (Rep. Kay Granger [R-Texas], Chair, and Rep. Rosa DeLauro [D-Connecticut], Ranking Member) will need to navigate demands from both ends of the political spectrum. Both are veterans in Congress and are long-time colleagues. The leaders of the Senate Appropriations Committee also are long-time colleagues and are both women: Patty Murray (D-Washington) is the Chair, and Susan Collins (R-Maine) is the Ranking Member.

Ms. Holohan highlighted that for the first time, the leaders of the House and Senate Appropriations Committees for both parties all are women, as is the Office of Management and Budget (OMB) Director, Ms. Shalanda Young, and they will be leading the debt limit negotiations. This group will have a challenging task for FY 2024. Among the concessions made by Speaker of the House Kevin McCarthy (R-California) was the open amendment process. Usually, legislation is considered in the House under a closed rule; not every member of the House offers amendments to a piece of legislation. In addition, Ms. Holohan noted that the House Appropriations Subcommittee on Labor, Health and Human Services, Education, and Related Agencies (Labor-HHS) has new leadership. Rep. Robert Aderholt (R-Alabama) is Chair of the House Appropriations Labor-HHS Subcommittee, and Rep. DeLauro is Ranking Member. Senator Tammy Baldwin (R-Wisconsin) is Chair of the Senate Labor-HHS Subcommittee, and Senator Shelly Moore Capito (R-West Virginia) is Ranking Member. Both Senators Baldwin and Capito are familiar with the NIH and NCI and have visited the NCI on the NIH campus.

Ms. Holohan explained that budget hearings are convening at a fast pace but are reduced in number. HHS Secretary Xavier Becerra has hearings the week of March 27, and Ms. Young, OMB Director, has been attending congressional hearings. The Secretaries' Cabinet-level hearings will convene for the first time. Funding bills are rarely enacted before the start of the fiscal year, with one exception in FY 2018, when the bill was combined with defense. Continuing resolutions (CRs) are anticipated, as well as short-term debt limit increases. One combination Congress might consider is an omnibus spending bill, which keeps many accounts and agencies flat-funded, similar to a CR, but can include increases for certain programs, and the NCI is optimistic that cancer research would be included in such a bill.

Ms. Holohan commented that oversight will be a major part of the 118th Congress. Hearings in the past week have included a House Energy and Commerce Committee session focusing on the federal response to COVID-19 and attended by the FDA Commissioner, CDC Director, and NIH's Dr. Lawrence Tabak, who performs the duties of the NIH Director. The House Committee on Oversight and Accountability convened a hearing to discuss the origins of the novel SARS-CoV-2 virus and laboratory leaks and held a COVID-19 session about the Paycheck Protection Act funding and fraudulent obtaining of these loans. She anticipates that these types of hearings will continue during the course of this Congress, noting that the appropriations hearings also present an opportunity for oversight.

In the discussion, the following point was made:

- In terms of considerations about labor costs and inflation and whether they factor into the federal budgeting process, the NCI acknowledges and requests funding to cover the cost of inflation but rarely receives it. Public witness opportunities are available in the budget hearings, and the academic research community can coordinate and make points about labor costs in an organized, unified way to congressional members, including Labor-HHS Subcommittees, who want to hear from professional groups that can provide clearer details on this situation. Congress is reviewing the NIH metrics and observing the number of grants, the success rates, and how funds are invested, as well as the deliverables and metrics. The NCI would like for clinical sites to be able to do more with the funding they receive.

V. ADAPTING NCI'S CLINICAL TRIALS SYSTEM TO A CHANGED CLINICAL RESEARCH ENVIRONMENT—DR. JAMES H. DOROSHOW

Dr. James H. Doroshow, Deputy Director for Clinical and Translational Research and Director, Division of Cancer Treatment and Diagnosis (DCTD), NCI, provided an update on initial and continuing effects of the pandemic environment on cancer clinical trials, as well as the NCI's 2030 strategic vision for clinical trials and activities to ameliorate current clinical research workforce issues.

Initial and Continuing Effects of the Pandemic Environment on Cancer Clinical Trials. From the start of the COVID-19 pandemic, several factors presented roadblocks to clinical trial accrual. These included the inability to conduct in-person study activities (e.g., informed consent, visits to receive investigational study drugs, assessments of patient safety and study adherence); lack of access to required imaging and laboratory facilities specified by trial documents; inability to collect low-grade adverse events despite potential lack of clinical relevance to study endpoints; and limited access to cancer care personnel and facilities. Complicating matters are the major ongoing issues of critical shortages of clinical research staff and essential health care workers and lack of institutional central research services. All have diminished trial availability and accrual, especially in underserved populations, and have led to substantive delays in reporting results.

To address these issues, the NCI switched to electronic consent, provided oral investigational agents directly to patients, initiated electronic study audits, and facilitated the use of telemedicine for study visits. The NCI also limited the impact of minor study deviations on trial conduct and evaluation; implemented decentralized testing for required laboratory and imaging studies; and developed a new strategic plan for NCI's clinical trials programs, which is now being implemented. Dr. Doroshow acknowledged the efforts of Dr. Worta McCaskill-Stevens, Chief, Community Oncology and Prevention Trials Research Group, Division of Cancer Prevention (DCP), NCI, and Dr. Margaret Mooney, Associate Director, Cancer Therapy Evaluation Program (CTEP), DCTD, NCI, in adapting the NCI's clinical trials system at the onset of the COVID-19 pandemic.

Dr. Doroshow reviewed the NCI clinical trials accrual rates from January 2020 through December 2022. The data source is the NCI's Clinical Trials Reporting Program (CTRP). From March to June 2020, a

major reduction to accruals was observed across trials, regardless of type. Although accruals in NCTN trials have recovered, investigator-initiated or externally peer-reviewed trials have not returned to pre-pandemic levels and remain 20 to 25 percent below target accruals. The primary reason for these differences is the remaining decreases in accrual to investigator-initiated trials at Cancer Centers. The NCI conducted a clinical trials workforce survey to assess the ongoing impact of the COVID-19 pandemic on the capacity of Cancer Centers to conduct treatment trials. The survey was administered by the Science Technology Policy Institute; 64 Cancer Centers participated, and the response rate was 100 percent. The results showed that the major issue affecting clinical trial capacity was that the lack of staff prevented opening the trials and accruing patients. The primary reason for staff attrition was the availability of higher pay or career advancement, followed by greater ability to work remotely and burnout from frontline work. Nearly 60 percent of individuals at academic Cancer Centers were recruited by pharmaceutical companies or contract research organizations, with only 10 percent retiring from active employment. Additionally, senior and recently trained staff also left Cancer Center employment, further reducing the pool of qualified candidates for new hires.

NCI's 2030 Vision for Clinical Trials: Strategic Planning Working Group Report. Dr. Doroshow summarized the Clinical Trials and Translational Research Advisory Committee (CTAC) Strategic Planning Working Group report on reassessing the strategic vision for clinical trials for 2030 and beyond and to reviewing and addressing necessary clinical trials infrastructure. The detailed report can be accessed from the NCI website. The key themes include trial complexity and cost, decentralized trial activities, accrual and access promotion, operational burden, new data collection approaches, and workforce outreach and training. The overarching goal of this strategic vision is to develop flexible, faster, simpler, less expensive, high-impact clinical trials that seamlessly integrate with clinical practice. The broad recommendations are to streamline processes for trial design and execution, decrease regulatory hurdles and broaden trial access, focus on essential endpoints, and increase efficiency of data collection. To address streamlining clinical trials, CTAC established the Streamlining Clinical Trials Working Group. In its 2022 interim report, this working group recommended limiting clinical trial data collection in late phase trials to essential data elements and using electronic health records (EHRs) to support clinical trials.

An analysis of recent NCTN phase 3 trials to assess data collections was performed. Dr. Doroshow noted some data elements to consider from an analysis of CTEP–sponsored trials, specifically late-phase, interventional treatment Investigational New Drug (IND)–exempt trials conducted in adults. The proposed categories include adverse events, medical history, concomitant medications, physical examination, laboratory testing, imaging and other assessment procedures, and patient-reported data. Several low-value data subcategories were highlighted, including low-grade adverse events, continuing to collect data for well-established drugs that have toxicity profiles that are well-known, and unrelated study endpoints or safety monitoring in laboratory data. The NCI's goals are to implement a set of standard practices for data collected in NCI phase 3 and phase 2/3 adult IND-exempt treatment trials and develop broad stakeholder engagement necessary for successful implementation of these standards. Dr. Doroshow highlighted a demonstration of the NCI's vision for clinical trials, the Pragmatica-Lung trial, which was developed and activated in 4 to 6 weeks and is designed to run 6 months, with a survival endpoint and essentially no adverse events except hospitalization.

Dr. Doroshow next described an NCI initiative on standardized EHR study builds, with the goal of facilitating development of standardized electronic treatment plan builds for NCI-supported clinical trials. The NCI launched a pilot project with 10 Cancer Centers, and two consortia have been established. The general approach is to develop standard representations of protocol-specified pharmacotherapy and other required therapeutic and assessment procedures. Efforts also will focus on developing a method for "packaging" the standardized requirements in a form that can either be imported directly into a site's EHR or facilitate local customization. The outcome will be a built library of modules that would be reusable

across trials and institutions.

NCI Activities to Ameliorate Current Clinical Research Workforce Issues. Dr. Doroshow highlighted ways that the NCI is proposing to address critical clinical trial workforce issues, including reducing the volume of trials that staff are responsible for supporting, improving alignment of institution and Cancer Center hiring processes related to staff recruitment and retention, and developing a virtual clinical trials office pilot study.

In the discussion, the following points were made:

- The NCI plans to continue the adapted clinical trials practices across its clinical trials groups (e.g., NCORP) that resulted from the responses to the COVID-19 pandemic.

- The character, complexity, and nature of clinical trials have changed over the last 10 years, especially with the advent of precision medicines and immunotherapies, but likely have not contributed to the decline in enrollment.

- Large EHR companies, including EPIC and Cerner**,** are participating in the NCI EHR study builds pilot project**,** and each group will need to adapt its EHR system to the study's template.

VI. RFA/COOP. AGR./RFP CONCEPTS—NEW AND RE-ISSUE—NCI PROGRAM STAFF

Office of the Director

Translational Research Toward Development of Kaposi Sarcoma Herpesvirus (KSHV) Vaccine (New RFA/Coop. Agr.)—Dr. Rebecca Liddell Huppi

Dr. Rebecca Liddell Huppi, Program Director, Office of HIV and AIDS Malignancy (OHAM), NCI, presented a new RFA concept on translational research toward development of a Kaposi Sarcoma Herpesvirus (KSHV) vaccine. This concept was developed in partnership with DCP, DCCPS, Division of Cancer Biology (DCB), and Center for Global Health (CGH). The purpose of this RFA is to support basic and translational research that will guide the development of a KSHV vaccine, with the goal of preventing or treating Kaposi Sarcoma (KS) and other KSHV-associated diseases. Dr. Huppi explained that KSHV is the causative agent of KS, which is a common malignancy in individuals with HIV/AIDS. Evidence to date indicates that oral fluids are the main route of KSHV spread, but many questions remain regarding the principal modes of transmission. In endemic areas (e.g., sub-Saharan Africa), acquisition of KSHV primarily occurs during childhood; in non-endemic areas, sexual transmission (particularly in men who have sex with men [MSM]) appears to be the primary route of transmission. Patients with epidemic KS (i.e., AIDS-related KS) continue to have a high mortality rate even in the era of combination antiretroviral therapy. In North America and most of Europe, overall KSVH seroprevalence is low, but there are concerns that the prevalence of KS might increase with the aging of MSM populations who are infected with KSHV, as classical KS is primarily a disease found in older people. Despite advances in the fields of epidemiology, virology, and immunology associated with KSHV, researchers have not been able to develop a successful KS prevention strategy for at-risk populations. Focused, sustained support for this area of science would reinvigorate the field and yield substantial benefits for at-risk populations in both North America and sub-Saharan Africa.

Dr. Huppi provided an overview of NCI efforts related to KSHV. In 2018, OHAM worked with the DCP, DCCPS, DCB, and CGH to develop an RFA titled "Investigation of the Transmission of KSHV" (RFA-CA-18-013) to advance knowledge of KSHV transmission. This RFA was re-issued in FY 2020 (RFA-CA-20-046). Nine R01 grants were awarded to address such areas as the initial steps in KSHV infection, biological factors protecting against such infection, and risk factors for KSHV transmission in endemic

and non-endemic areas. The NCI BSA *ad hoc* Subcommittee on HIV and AIDS Malignancy has been defining gaps in the understanding of KSHV transmission and infection since it was first convened in 2017. After the 2018 KSHV RFA, the NCI BSA *ad hoc* Working Group on Immunology of Therapies and Vaccines and Research Structure recommended further exploration of potential approaches to developing a vaccine against KSHV. This recommendation was enthusiastically endorsed by the BSA Subcommittee and the BSA. In October 2021, OHAM held a virtual state-of-the-science workshop that included expertise across the spectrum of HIV, oncology, virology, vaccinology, and immunology. Workshop discussions ranged from knowledge gaps regarding KSHV epidemiology to lessons learned from the development of other viral vaccines. Despite possible challenges to developing and implementing such a vaccine, the consensus view was that the public health benefits would make the KSHV vaccine a worthwhile endeavor.

A portfolio analysis revealed two active research project grants that specifically address KSHV vaccine development. In FY 2021 and FY 2022, 56 NCI-funded grants addressed KS or KSHV—9 of which were funded through RFA-CA-18-013 and RFA-CA-20-046. Six NCI-funded grants addressed issues that potentially could be important in vaccine development. Other NIH ICs funded 17 grants that address KS or KSHV. When compared to a portfolio review of other NIH ICs performed in FY 2015 and FY 2016, this represented a reduction of investment in KS or KSHV research by more than 50 percent.

This RFA will support research related to (1) the initial steps of infection with KSHV and the primary means of transmission that can be targeted with a vaccine in different populations; (2) identification and evaluation of KSHV structural and nonstructural targets for a potential KSHV vaccine; (3) development of animal models to study prototype KSHV vaccines; (4) development and testing of candidate KSHV vaccines; (5) studies to optimize the efficacy of a KSHV vaccine for people with HIV; and (6) standardization or optimization of KSHV detection methods. Funding for this RFA will be made available through the NCI AIDS budget of the NIH Office of AIDS Research.

Subcommittee Review. Dr. Dorothy K. Hatsukami, Associate Director of Cancer Prevention and Control, Forster Family Chair in Cancer Prevention, Masonic Cancer Center, Professor, Department of Psychiatry and Behavioral Sciences, University of Minnesota, expressed the Subcommittee's strong support for the concept, which represents a multi-collaborative effort across the NCI Divisions and Centers. The Subcommittee appreciated NCI staff responses to its concerns on the potential overlap among targeted areas of the prior KHSV RFA, questions on whether the results from the prior RFA might help inform this future research, and clarifications on clinical trials. The Subcommittee suggested incorporating a data-sharing requirement into the RFA, the rationale being that data generated by U01 investigators should be shared within the consortium and with other investigators conducting research in this particular area.

In the discussion, the following points were made:

- Expanding the RFA to include proposals from investigators outside the U01 network who already are conducting KSHV vaccine research will increase the impact of this effort.

- Research on Epstein–Barr virus (EBV) vaccines is expected to help inform the development of the KSHV vaccine. Importantly, unlike EBV, KSHV is only transmitted in particular settings—indicating that minimal enhancement of the immune response to KSHV likely will be required to generate an effective vaccine.

- An effective KSHV vaccine has major implications for vulnerable populations in sub-Saharan Africa and other locations (e.g., western China). The vaccine should be affordable in these regions, and strategies for delivering the vaccine to these locations should be prepared.

The first-year cost is estimated at $6 M for six to eight U01 awards, with total cost of $30 M for 5 years.

Motion. A motion to approve the Office of the Director's (OD) RFA/Coop. Agr. entitled "Translational Research Toward Development of Kaposi Herpesvirus (KSHV) Vaccine" was approved unanimously.

Division of Cancer Treatment and Diagnosis

Targeting Fusion Oncoproteins in Childhood Cancers (TFCC) Network

(New RFA)—Dr. Malcolm A. Smith

Dr. Malcolm A. Smith, Associate Branch Chief, Pediatric Oncology, Clinical Investigations Branch CTEP, DCTD, NCI, presented a new RFA concept to establish the Targeting Fusion Oncoproteins in Childhood Cancers (TFCC) network, which was developed in collaboration with the DCB. Dr. Smith emphasized the importance of active targeted agents for improving the outcomes of childhood cancers and reviewed data from the National Childhood Cancer Registry. Over the past 21 years, the mortality rates of childhood acute lymphoblastic leukemia declined 50 percent, attributed to the advent of agents such as inhibitors to fusion oncoprotein BCL-ABR 1 and to chimeric antigen receptor (CAR) T-cell therapy. The mortality rates of non-Hodgkin lymphoma declined 60 percent during this same period, with the discovery of cluster of differentiate 20 (CD-20) targeted monoclonal antibodies and similar agents, and the rates of mortality of Hodgkin lymphoma declined 80 percent, attributed to next-generation CD-20 agents (e.g., brentuximab vedotin). Conversely, during this same time period, the decline in mortality rates for soft tissue (e.g., rhabdomyosarcoma) and bone cancers (e.g., osteosarcomas, Ewing sarcomas) was minimal, illustrating that active new agents are urgently needed for these cancers to enable a cure in children and adults. Many of the current hard-to-treat cancers for which there has been little progress are driven by fusion oncoproteins.

This concept builds on the Cancer Moonshot Fusion Oncoproteins in Childhood Cancers (FusOnC2) Consortium, which consists of nine U54 grants investigating six different fusion oncoproteins. The biology being studied includes chromatin remodeling, phase separation, model development, proteolysis targeting chimeras, novel chemoproteomic strategies, and critical dependencies. Dr. Smith highlighted the advances made through the FusOnC2 Consortium but did not have time to describe all in detail. FusOnC2 investigators identified a ubiquitin ligase, TRIM8, that regulates fusion oncoprotein EWS-FLI1 levels; small molecules that stabilize the autoinhibited conformation of FLI1 and other erythroblast transformation–specific family transcription factors; menin as a critical dependency in nucleoporin 98-rearranged leukemias; and, just recently, ETV-6 as a critical dependency for Ewing sarcoma with EWS-FLI1. Investigators also developed high-penetrance zebrafish genetic models of Ewing sarcoma, which show multiple similarities to human Ewing sarcoma and can be used for drug screening. External scientific consultants conducted a review of the progress of the FusOnC2 Consortium to advise the NCI on next steps. The recommendations were to continue research in this area; diversify the fusion oncoproteins studies in future efforts; apply state-of-the-art chemoproteomic methods to directly targeting fusion oncoproteins; and decouple the chemical biology expertise from that of the basic science projects to provide drug discovery expertise to the entire network of investigators. To determine interest in pursuing this research, the NCI hosted a webinar series titled "Novel Chemical Approaches for Targeting Fusion Oncoproteins" in fall 2022. Nearly 1,000 individuals registered and heard presentations on diverse technologies and approaches.

The NCI is proposing to establish a TFCC network consisting of two components: (1) projects to better understand the mechanisms of fusion-driven oncogenesis and (2) next-generation chemistry centers for fusion oncoproteins (FusOnC NGC), using the U01 and UM1 funding mechanisms, respectively. The U01 projects will focus on identifying novel drug targets and critical dependencies across various activities, including dissecting pathways by which these fusion oncoproteins cause cancer or determining

the roles of non-coding RNAs or post-translational modifications in their function. The UM1 grants will allow teams with complementary research and expertise to collaborate toward the common goal of identifying and developing small molecules that can disrupt the activity of fusion oncoprotein drivers. Possible research topics include identifying inhibitors of fusion oncoprotein activity, blocking critical interactions, or selectively degrading the fusion oncoproteins or their critical dependencies.

The TFCC network's organizational structure will be composed of a steering committee, associate members, and patient advocates. To encourage collaboration across the Network, the UM1 budget will consist of a 15 percent set-aside in years 2–5 of the award cycle. Additional considerations from the BSA reviewers related to fusion oncoproteins that have a high risk of treatment failure and encouraging data sharing and collaborating across other NCI programs (e.g., CCDI) have been incorporated into the RFA. Markers of success will be the number of new collaborations established; functional domains, critical dependencies, and vulnerabilities identified; and technologies and strategies identified for targeting fusion oncoproteins or their dependencies. The NCI anticipates that chemical probes or tools developed in the TFCC will advance to further optimization as new drug candidates.

Subcommittee Review. Dr. Jennifer R. Grandis, Robert K. Werbe Distinguished Professor in Head and Neck Cancer, University of California, San Francisco, expressed the Subcommittee's enthusiasm and support for the concept, which builds upon the successes and lessons learned in the FusOnC2 Consortium. Dr. Grandis commented that the webinar series demonstrated a high level of engagement for this research and that this concept is a logical next step. She conveyed the Subcommittee's enthusiasm in the NCI's use of the UM1 mechanism, incentives for further collaborations, and the potential for leveraging the NIH National Center for Advancing Translational Sciences' National COVID Cohort Collaborative approach among the Cancer Centers. The Subcommittee emphasized the opportunity to collect, aggregate, and harmonize data in the TFCC network, setting an example for similar initiatives.

In the discussion, the following point was made:

- The NCI has established the Pediatric Immunotherapy Network (PIN), which specifically investigates immunological approaches to treating childhood cancers, including fusion oncoproteins, and those approaches will not be addressed in this RFA.

The first-year cost is estimated at $1.825 M for six U01 awards and two UM1 awards, with a total cost of $8.3 M for 5 years.

Motion. A motion to approve the DCTD's RFA entitled "Targeting Fushion Oncoproteins in Childhood Cancers (TFCC) Network" was approved unanimously.

Cooperative Human Tissue Network (CHTN) (Re-Issue RFA/Limited Competition/Coop. Agr.)—Dr. Rodrigo Chuaqui

Dr. Rodrigo Chuaqui, Program Director, DCTD, NCI, presented a re-issue limited competition RFA concept for continuing the Cooperative Human Tissue Network (CHTN), which is a resource to procure high-quality samples for basic and early translational research. The CHTN was established in 1987 and consists of five adult divisions and one pediatric division that distributes samples across all geographical areas. Each of the adult divisions works with two to six remote-site hospitals to increase the procurement capacity. The pediatric division procures samples from 90 percent of pediatric hospitals in the United States. The CHTN is a unique public biospecimen resource available to the broader scientific community that prospectively procures samples, mostly during primary surgeries, in response to a researcher's questions. The Network allows for a wide range of samples to be collected, including rare specimens that are distributed with basic demographic and histopathology information. Fresh and frozen samples, which are generally limited in biorepositories, constituted approximately 50 percent of samples shipped in the

past 5 years. The CHTN provides easy access to samples and at low cost.

Dr. Chuaqui highlighted the Network's accomplishments. From 2017 to 2021, the CHTN distributed 175,000 samples to 1,849 individual researchers; 77 percent were academic investigators, 66 percent were R01 grantees, 18 percent were from industry, and 5 percent were government researchers. During this period, CHTN participants produced 500 publications and 55 patents. This re-issuance RFA will support continuing the CHTN to provide high-quality specimens to a cadre of researchers in academia, industry, SPORES, and Cancer Centers, as well as NIH intramural researchers. CHTN samples support a wide range of current high-throughput technologies, including genomics and transcriptomics. An external review of the program was conducted in June 2022, and the five reviewers were in consensus on the high value of the CHTN to the research community, especially to R01 grantees. The CHTN and has no alternative network of its kind. Commercial resources usually cannot supply the full range of services or types of samples and at low cost. Because the cost of operations has increased in the past 5 years, including the number requests for and the types of samples, an increase is funding is being requested.

Subcommittee Review. Dr. Shelton Earp, Director, University of North Carolina (UNC) Lineberger Comprehensive Cancer Center, Director UNC Cancer Care, The University of North Carolina at Chapel Hill, expressed the Subcommittee's enthusiasm and support for the concept. Dr. Earp suggested exploring a cost structure model that includes industry participation. The Subcommittee was impressed with the accomplishments of the Network and further suggested investigating approaches to increase minority accruals in the CHTN.

In the discussion, the following points were made:

- The request for increasing the budget is to support procurement and the labor to prepare and distribute the samples, but not administrative costs.

- In the six primary CHTN institutions, any surgery that generates tissue remnants after clinical care is considered a candidate to be a CHTN sample if requested. Only rare tumors or difficult-to-obtain samples are stored because most of the distribution of samples comes from a prospective procurement.

The first-year cost for the one-time issuance is estimated at $6.2 M for six U24 awards, with a total cost of $31 M for 5 years.

Motion. A motion to concur on the re-issuance of the DCTD's RFA/Limited Competition/Coop. Agr. entitled "Cooperative Human Tissue Network (CHTN)" was approved with 21 ayes, 0 nays, and 5 abstentions.

Office of the Director

FY 2024 NCI Small Business Innovation Research (SBIR) Contract Topics (R43) (New RFP)— Dr. Monique Pond

Dr. Monique Pond, Program Director, SBIR Development Center, presented 11 Small Business Innovation Research (SBIR) research and development (R&D) contract topics for funding in FY 2024. The NCI SBIR budget is a congressionally mandated set-aside allotment of the overall NCI appropriations. The SBIR program supports promising startup companies with SBIR and Small Business Technology Transfer (STTR) grants that are investigator initiated and SBIR contracts. In FY 2022, the NCI allocated $20 M of the budget to R&D contracts; this amount can vary from year to year. The NCI does not prescribe any fixed dollar amount for grants versus contracts but focuses on funding the best translational science that will help patients with cancer. With the contract mechanism, the NCI is able to

define narrowly focused topics that have specific product development goals and milestones, which is in contrast to the grant mechanism. Dr. Pond noted that the funding for the SBIR/STTR awards does not affect the RPG pool.

R&D contracts are used to stimulate commercialization in emerging areas; streamline stepwise product development; and support technology transfer from NIH laboratories to industry. The contract topics are diverse and serve needs beyond just the NCI. All products developed must fulfill a commercial need. Contract proposals undergo a rigorous peer-review process, and the reviews are conducted by NCI DEA as opposed to the NIH Center for Scientific Review. In addition, contract proposals must align with the specific topic and the deliverables that are detailed in the solicitation.

Identifying the contract topics is an NCI-wide process. Each October, the SBIR Development Center solicits ideas for new contract proposals from across the NCI. Topics are submitted from program directors from the NCI Divisions, Offices, and Centers and also from the FDA Center for Devices and Radiological Health. Submitted topics then are evaluated by two NCI technology advisory group (TAG) panels: TAG 1 focuses on therapeutic diagnostics and molecular analysis technologies, and TAG 2 reviews radiation therapies, medical devices, and health information technology (IT) and bioinformatics. The TAG panels are composed of subject-matter experts from across the NCI, who evaluate the submitted topics for innovation and concept; commercialization potential; and the ability to have a significant benefit for cancer patients, providers, and caregivers. The reviewers ensure that no duplication exists in the NCI SBIR portfolio and that re-issued topics are justified appropriately.

The 11 SBIR R&D contract topics were selected from 18 that were submitted and reflect NCI priority areas, commercial potential, and portfolio gaps. These fall into the areas of medical devices, diagnostics, and IT and biotechnology. Eight of the 11 topics have also been approved by the NCI Implementation Coordinating Committee as having Moonshot relevance. Dr. Pond summarized the 11 topics and overall goals, noting that detailed reports have been provided in the electronic Board book.

Medical Devices Topics

Ultra-Fast Dose Rate (FLASH) Radiation Detectors and Safety Systems for Cancer Treatment. Advance the development of devices for evaluating FLASH radiation therapy and translating this therapy into the clinic.

Clinical Diagnostics and Molecular Analysis Topics

Technologies for Detecting Tumor-Derived Cell Clusters. Support the development of *in vitro* technologies that can enumerate and identify cell types in tumor-derived cell clusters, with or without enrichment, to better understand the biology and role of different cells in cancer metastasis

Rapid and Affordable Point-of-Care HPV Diagnostics for Cervical Cancer Control. Advance the development of new alternatives for HPV testing to the market that are both in a form and at a price point that will enable self-testing programs to be established globally. Re-issue topic.

Translation of Novel Cancer-Specific Imaging Agents and Techniques to Mediate Successful Image-Guided Cancer Interventions. Support the translation of novel activatable agents and techniques for sensitive cancer detection in human subjects. Re-issue topic.

Microbiome-Based Tests for Cancer Research, Diagnosis, Prognosis, and/or Patient Management. Support the development of innovative tests for early cancer detection and diagnosis, prognosis, and/or treatment assignment to be used in research.

Organ-on-Chip for Preclinical and Translational Radiological Studies. Support the development and validation of organ-on-chip devices for research and preclinical applications in studies with radiation and drug radiation combinations.

Point-of-Care Detection of Prostate Specific Antigen (PSA). Advance the development of a home PSA test at an appropriate price point.

Information Technology and Bioinformatics Topics

Cancer Prevention and Treatment Clinical Trials Tools for Recruitment and Retention of Diverse Populations. Support the development of a digital platform that provides primary care physicians with validated cancer risk assessment tools, cancer prevention guidelines, and clinical recommendations based on a patient's risk factors. Re-issue topic.

Cloud-Based Multimodal Data Analysis Software for the Cancer Research Data Commons (CRDC). Advance the evolution of cloud-based multimodal informatics tools to integrate with the CRDC for broader user community engagement. Re-issue topic.

Evaluation Data Sets as Medical Device Development Tools (MDDTs) for Testing Cancer Technologies. Stimulate the participation of small businesses in the FDA's MDDTs program to develop datasets that can be used to assess medical devices in oncology settings. Re-issue topic.

Automated Software for Point-of-Care Testing to Identify Cancer-Associated Malnutrition. Facilitate the commercial development of novel automated point-of-care nutrition screeners that combine first-line questionnaires with automated segmentation from diagnostic imaging (e.g., from repurposed computed tomography images) to detect malnutrition risk early and repeatedly during cancer care and in cancer populations with higher prevalence of malnutrition.

SBIR R&D Contracts: Impact and Success Stories

Dr. Pond emphasized that the SBIR R&D contracts have supported the successful commercialization of many products used for diagnosing, monitoring, or treating patients with cancer, such as DiaCarta's RadTox™ and Medable, Inc.'s brachytherapy device. An analysis of the SBIR R&D contracts portfolio from 2013 to 2018 revealed that approximately 20 percent of funded projects have resulted in commercialized products, with more than 30 percent in 2013 alone. These findings are similar to the SBIR grants portfolio. The NCI considers contracts an important mechanism for NCI funding and one way to enable innovative products reaching the clinic for patients with cancer.

Subcommittee Review. Dr. Karen E. Knudsen, Chief Executive Officer, American Cancer Society, Inc., American Cancer Society Cancer Action Network, expressed the Subcommittee's enthusiasm and strong support for the concept. The Subcommittee appreciated NCI staff responses to their questions on topic selections and priorities and coordination with SBIR-like mechanisms across the NIH. The Subcommittee also commended the NCI for the overall innovation and success of the program, including the high number of products moving to commercialization.

In the discussion, the following points were made:

- Diversity is an important part of the SBIR Development Center's mission and goals and also is reflected in the contract topics. In 2019, the SBIR Development Center launched the Applicant Assistance Program (AAP), focusing on mentoring and training of new entrepreneurs. Nine cohorts have completed the AAP, and the majority of awards have been made to underrepresented populations in the biomedical sciences.

- The SBIR Development Center worked with DCP staff on their topic to solicit applications addressing cervical cancer in an effort to develop point-of-care delivery technologies implementable in global health settings for rapid testing in order to provide treatment to women in need. Some of the modalities within this scope could potentially be adapted for self-sampling or at-home use under the right situations.

Motion. A motion to approve the OD's RFP entitled "FY 2024 NCI Small Business Innovation Research (SBIR) Contract Topics (R43)" was approved unanimously.

VII. ONGOING AND NEW BUSINESS—DR. KEITH T. FLAHERTY

Members were asked to forward suggestions for potential future agenda items to Drs. Flaherty and Gray.

VIII. ADJOURNMENT—DR. KEITH T. FLAHERTY

There being no further business, the 7th virtual meeting of the BSA was adjourned at 4:52 p.m. on Tuesday, 21 March 2023.

Date	Keith T. Flaherty, M.D. Chair, Board of Scientific Advisors
Date	Paulette S. Gray, Ph.D. Executive Secretary, Board of Scientific Advisors