

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
NATIONAL CANCER INSTITUTE
10th VIRTUAL NATIONAL CANCER ADVISORY BOARD**

**Summary of Meeting
February 12, 2019**

**Virtual
Conference Room TE406, East Wing, Shady Grove Campus
National Cancer Institute
National Institutes of Health
Bethesda, Maryland**

**NATIONAL CANCER ADVISORY BOARD
BETHESDA, MARYLAND
Summary of Meeting
February 12, 2019**

The National Cancer Advisory Board (NCAB) convened for its 10th virtual regular meeting on February 12, 2019. NCAB members attended virtually, and National Cancer Institute (NCI) staff attended in Conference Room TE406, East Wing, Shady Grove Campus, National Institutes of Health (NIH), Bethesda, MD. The meeting was open to the public on Tuesday, February 12, 2019, from 1:00 p.m. to 3:30 p.m., and closed to the public from 3:45 p.m. to 4:19 p.m. The NCAB Chair, Dr. Elizabeth M. Jaffee, Deputy Director, The Sidney Kimmel Comprehensive Cancer Center, Co-Director, Skip Viragh Center for Pancreas Cancer, The Dana and Albert “Cubby” Broccoli Professor of Oncology, Johns Hopkins University, presided during both the open and closed sessions.

NCAB Members

Dr. Elizabeth M. Jaffee (Chair, attended in person)
Dr. Peter C. Adamson
Dr. Francis Ali-Osman
Dr. Deborah Watkins Bruner (absent)
Dr. Yuan Chang
Dr. David C. Christiani
Dr. Judy E. Garber
Mr. Lawrence O. Gostin
Dr. Scott W. Hiebert
Dr. Beth Y. Karlan
Dr. Timothy J. Ley
Dr. Electra D. Paskett
Dr. Nancy J. Raab-Traub
Dr. Mack Roach, III
Dr. Charles L. Sawyers
Dr. Margaret R. Spitz
Dr. Max S. Wicha

Members, Scientific Program Leaders, National Cancer Institute, NIH

Dr. Norman E. Sharpless, Director, National Cancer Institute
Dr. L. Michelle Bennett, Director, Center for Research Strategy
Dr. Stephen J. Chanock, Director, Division of Cancer Epidemiology and Genetics
Dr. Henry P. Ciolino, Director, Office of Cancer Centers
Dr. Robert Croyle, Director, Division of Cancer Control and Population Sciences and Interim Director,
Center for Global Health
Dr. William Dahut, Scientific Director for Clinical Research, Center for Cancer Research
Dr. James H. Doroshow, Deputy Director for Clinical and Translational Research
Dr. Dan Gallahan, Deputy Director, Division of Cancer Biology
Mr. Peter Garrett, Director, Office of Communications and Public Liaison
Dr. Paulette S. Gray, Director, Division of Extramural Activities
Dr. Ed Harlow, Special Advisor to the Director
Dr. Toby T. Hecht, Deputy Director, Division of Cancer Treatment and Diagnosis
Dr. Tony Kerlavage, Acting Director, Center for Biomedical Informatics and Information Technology
Dr. Kristin Komschlies, Acting Director, Office of Scientific Operations, NCI Campus at Frederick
Dr. Douglas R. Lowy, Deputy Director, National Cancer Institute
Dr. Glenn Merlino, Scientific Director for Basic Research, Center for Cancer Research
Dr. Tom Misteli, Director, Center for Cancer Research
Dr. Henry Rodriguez, Acting Associate Director, Center for Strategic Scientific Initiatives
Mr. Jeff Shilling, Acting Chief Information Officer and Chief of Infrastructure and Information
Technology Services Branch, Center for Bioinformatics and Information Technology
Ms. Donna Siegle, Executive Officer, and Deputy Director for Management
Dr. Dinah Singer, Acting Deputy Director and Director, Division of Cancer Biology
Dr. Sanya Springfield, Director, Center to Reduce Cancer Health Disparities
Dr. Louis M. Staudt, Director, Center for Cancer Genomics
Mr. Michael Weingarten, Director, Small Business Innovation Research and Small Business Technology
Transfer Programs
Dr. Jonathan Wiest, Director, Center for Cancer Training
Dr. Deborah Winn, Acting Director, Division of Cancer Prevention
Dr. Robert Yarchoan, Director, Office of HIV and AIDS Malignancy
Dr. Maureen Johnson, Executive Secretary, Office of the Director

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TUESDAY, 12 FEBRUARY 2019**I. CALL TO ORDER AND OPENING REMARKS— DR. ELIZABETH M. JAFFEE**

Dr. Elizabeth M. Jaffee called to order the 10th virtual National Cancer Advisory Board (NCAB) meeting. She welcomed members of the Board, staff, and guests. Members of the public were welcomed and invited to submit to Dr. Paulette S. Gray, Director, Division of Extramural Activities (DEA), National Cancer Institute (NCI), in writing and within 10 days, any comments regarding items discussed during the meeting. Dr. Jaffee reviewed the confidentiality and conflict-of-interest practices required of Board members in their deliberations. She also thanked NCI Information Technology and DEA Committee Management Office (CMO) staff for setting up the infrastructure for the virtual meeting.

Motion. A motion to accept the minutes of the December 4, 2019 Joint Meeting of the Board of Scientific Advisors (BSA) and the NCAB was approved unanimously.

II. FUTURE BOARD MEETING DATES—DR. ELIZABETH M. JAFFEE

Dr. Jaffee called Board members' attention to the future meeting dates listed on the agenda.

III. NCI DIRECTOR'S REPORT—DR. NORMAN E. SHARPLESS

Dr. Norman E. Sharpless, Director, NCI, welcomed NCAB members and attendees to the 10th virtual meeting and provided an update on childhood cancer research, the NCI budget, Cancer MoonshotSM initiative, and new and ongoing activities.

NCI Childhood Cancer Research. Dr. Sharpless remarked on the February 5, 2019 State of the Union Address in which the President announced a \$500 million (M) initiative for new pediatric cancer research. The NCI recognizes a responsibility to better address the childhood cancer burden in the United States and is actively discussing and planning new efforts to support this new national effort. Dr. Sharpless highlighted some of the current initiatives of NCI's childhood cancer research portfolio, which conveys the ongoing commitment in this area. The cellular immunotherapy research infrastructure for conducting chimeric antigen receptor (CAR) -T cell clinical trials is being developed in the Frederick National Laboratory for Cancer Research (FNLCR). The Children's Oncology Group (COG) has been conducting clinical trials in pediatric populations, including the NCI and COG Pediatric Molecular Analysis for Therapy Choice (Pediatric MATCH) trial, which leverages the adult NCI-MATCH. The Pediatric Preclinical Testing Consortium has been using animal models of childhood cancer for therapeutic testing for more than a decade. There have been strong ongoing efforts in childhood cancer in the NCI Intramural Research Program (IRP). Certain cancers have been treated with the potential for a cure in the Pediatric Oncology Branch in the Center for Cancer Research (CCR). In addition, the NCI has supported implementation of two recently approved legislative initiatives—the Childhood Cancer Survivorship, Treatment, Access and Research (STAR) Act and the Research to Accelerate Cures and Equality (RACE) for Children Act—both of which include childhood cancer components. Dr. Sharpless explained that these initiatives are not all-inclusive of the ongoing pediatric cancer research efforts and called attention to the Childhood Cancer Survivor Study on long-term effects and mortality. Childhood cancer is one area that the NCI has long supported and an area in which more can be done.

NCI Budget. Dr. Sharpless reported that having an earlier decision of the fiscal year (FY) 2019 budget allowed the NCI a full year to compose budgetary and planning decisions. NCAB members were informed that in FY 2019, the NCI had the highest increase in competing (Type 2) R01 applications of all the National Institutes of Health (NIH) Institutes or Centers (ICs). From FYs 2009 to 2018, the overall increase in Type 2 R01 applications to the NCI was 60 percent, whereas other ICs had modest increases. The average increase in R01 applications across the United States is 10 percent. The NCI was the clear

outlier, even exceeding the 30 percent growth of two ICs receiving substantial funding for Alzheimer's disease: the National Institute of Neurological Disorders and Stroke (NINDS) and the National Institute on Aging (NIA). Despite a 20 percent increase in the NCI budget for this time period, this increase has not been at the same pace as the increase in the number of R01 applications received, thus resulting in decreased paylines. The NCI has implemented funding strategies for FY 2019 to assist in preserving paylines. In the Research Project Grant (RPG) Pool, Type 2 grants will be awarded with a 19 percent reduction below the committed funding level and Non-Competing Continuation (Type 5) grants will be awarded at a 3 percent reduction. Also, there will be a 5 percent across-the-board reduction in funding for NCI Divisions, Offices, and Centers.

Dr. Sharpless explained that should the trends in R01 applications continue, these strategies will not be sustainable without further increases in NCI regular appropriations. Although this news on funding is less than desirable for investigators, especially those applying for a first R01, the influx of new scientists and new ideas about cancer into the NCI has been positive. To address this important topic at length, the NCI in the next few months will conduct an internal analysis of the RPG pool, future planning, and funding. NCI Deputy Director, Dr. Douglas R. Lowy, will lead this effort, and reports to the NCAB will be forthcoming.

Dr. Sharpless was pleased to report that on January 25, 2019, the NCI hosted its first Facebook Live and Twitter Live events—"NCI's 2019 Plans: Conversation with the NCI Director"—which focused on budgetary issues, including the FY 2019 funding strategies and paylines. Dr. Sharpless was joined for the event by BSA Chair Dr. Dafna Bar-Sagi and NCAB Chair Dr. Jaffee, who moderated the conversation.

NCI Cancer MoonshotSM Initiative. Dr. Sharpless reminded the NCAB members that the Cancer MoonshotSM appropriation of \$400 M for FY 2019 will be the highest of the \$1.8 billion (B), 7-year funding period for the program. Beginning in FY 2020, the annual allotments will decrease by \$200 M per year. The NCI has funded initiatives covering each of the 10 NCAB Blue Ribbon Panel (BRP) recommendations. An initial Cancer MoonshotSM portfolio analysis has been completed, revealing the robust number of new groups of investigators and new scientific endeavors. Scientific results are beginning to be reported. Some of the new networks and consortia are starting to take shape, including the recently funded Immuno-Oncology Translational Network, Pediatric Immunotherapy and Development Network, and Human Tumor Atlas Network. Kickoff meetings with research teams for these networks and NCI program staff are in progress. Dr. Sharpless highlighted a recent report on cervical cancer control and automated visual evaluation for cancer screening published in the January 2019 issue of the *Journal of the National Cancer Institute*, which resulted from the BRP recommendation on prevention and early detection. The NCAB BRP and Beau Biden Foundation recently were updated on the Cancer MoonshotSM progress, and Dr. Sharpless routinely meets with members of the NIH *All of Us* Research Program Advisory Panel.

Ongoing NCI Activities. Dr. Sharpless told NCAB members that the NCI is a major customer of the NIH Clinical Center (Clinical Center). Overall the inpatient volume and facility utilization are low for a 200-bed hospital. Usage has improved somewhat in the past few years, but has now reached a plateau. Visits to the outpatient clinic and the day center are busy and strong. Discussions have been ongoing with the Clinical Center CEO, Dr. James K. Gilman, about ways to increase the inpatient use and attract clinical trials that leverage the Clinical Center expertise and are a good fit for the NCI IRP, including CAR-T cell trials.

Dr. Sharpless announced his participation in two advisory groups: (1) chair of the Clinical Center Governing Board (CCGB) and (2) member of the newly formed Advisory Committee to the NIH Director (ACD) Working Group on Changing the Culture to End Sexual Harassment. He reflected on the life of

Dr. Steven I. Katz, who was Chair of the CCGB and Director of the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) until his passing on December 20, 2018. The mission of the ACD Working Group on Sexual Harassment aligns with recommendations of the 2018 National Academies of Sciences, Engineering, and Medicine report on *Sexual Harassment of Women in Academic Sciences, Engineering, and Medicine*, which the NIH co-sponsored. Updates on NIH policies and approaches to prevent and address sexual harassment internally have been launched. The policies that the NIH can adopt as a federal agency to address the sexual harassment culture/climate externally are limited, and NIH Director Dr. Francis S. Collins convened the ACD Working Group on Sexual Harassment to solicit input from the extramural community. After a series of meetings and deliberations, recommendations will be reported to Dr. Collins in summer 2019.

NCAB members were reminded that the rapid contracting structure of the FNLCR supports the NCI IRP research and launches new large-scale national projects. The RAS Initiative is in its sixth year of funding and has generated new scientific advances. The National Cryo-Electron Microscopy Facility is widely used in the extramural community. The recent CAR-T cell production facility, which will support IRP trials initially and later expand to the extramural community, is operational. The NCI–Department of Energy collaborations are underway. The NCI anticipates continuing on this positive trajectory at the FNLCR as a federally funded research and development center and making good use of this diverse research portfolio and resources. In August 2019, the FNLCR will begin operating under a bridge award. Discussions on the contract recompetete process are planned.

Dr. Sharpless explained that the NCAB *ad hoc* SBIR Working Group, one of three established shortly after his becoming NCI Director, has completed its report of the NCI SBIR Program, which will be presented later in the meeting. Dr. Sharpless reflected on his prior experience with the NIH/NCI SBIR program, including starting spinoff companies, consulting for other companies and faculty, and navigating basic science into clinical practice. The NCI SBIR/STTR program is a large investment for the NCI and in evaluating its returns, the NCI sought external advice on its SBIR activities.

Dr. Sharpless remarked on NCI's efforts to improve communications to the external research community. In 2018, the NCI established a Digital Communications Assessment Working Group to evaluate NCI's internet presence and website analytics. The aim was to assess how the external community interacts with and receives information from the NCI. Mr. Peter Garrett, Director, Office of Communications and Public Liaison, served as Chair and guided the group's activities. Data have been presented and discussed with NCI leadership and recommendations proposed.

Dr. Sharpless noted NCI's ongoing recruitment efforts for directors for the Center for Global Health, Center for Biomedical Informatics and Information Technology, Cancer Therapy Evaluation Program (CTEP), and Division of Cancer Prevention (DCP), as well as for the Associate Director of the FNLCR. Candidate pools are strong, and interviews and vetting per federal procedure are in process.

Dr. Sharpless announced that the 2019 National Foundation for Cancer Research Szent-Györgyi Prize for Progress in Cancer Research was awarded to Dr. Steven A. Rosenberg, CCR, for his pioneering role in the development of adoptive immunotherapy to treat cancer.

Questions and Answers

Dr. Max S. Wicha, Madeline and Sidney Forbes Professor of Oncology, Director, Forbes Institute for Cancer Discovery, Founding Director Emeritus, University of Michigan Rogel Cancer Center, and Professor of Internal Medicine, Division of Hematology and Oncology, University of Michigan, asked about any additional cuts to R01s being forecast. Dr. Sharpless explained that because of the increase in R01 applications for FY 2019, the NCI decided to take measures to preserve the paylines, which included

increasing cuts to the Type 2 and Type 5 awards. Other steps taken to free up capital in FY 2019 include ending some initiatives, decreasing funding across the NCI, and postponing funding for FY 2020 in areas that could support a delay. The changes are intended to allow the NCI to devote resources to top priorities, such as the RPG Pool. The Cancer MoonshotSM funding will be held in reserve for Moonshot initiatives. A significant amount of the FY 2019 regular appropriations will continue to support the RPG pool. In this budget climate, unless the trend in R01 applications decreases or the NCI regular appropriations increase, NCI's current approaches will be untenable in the long term.

Dr. Timothy J. Ley, Professor of Medicine and Genetics, Division of Oncology, Department of Medicine, Washington University School of Medicine in St. Louis, suggested investigating other strategic approaches to increase funding for cancer grants outside of the NCI to accommodate the increasing rate of R01 applications/funding supply/demand ratio. Dr. Sharpless noted the enthusiasm among other ICs to fund cancer grants, primarily in the area of basic research, and ongoing discussions on establishing co-funding structures with other ICs via the Center for Scientific Review (CSR) process.

Dr. Judy E. Garber, Director, Center for Cancer Genetics and Prevention, Dana-Farber Cancer Institute, Professor of Medicine, Harvard Medical School, asked whether any changes were proposed to the funding distribution at the FNLCR, given the plans to increase activities. Dr. Sharpless explained that the overall FNLCR budget fluctuates and depends on what the NCI does. The general consensus among prior NCI Directors is that the FNLCR has a mission that is vital to the NCI, and the NCI is actively discussing the current and future state of the operation of the FNLCR. Dr. Sharpless also noted that the Frederick National Laboratory Advisory Committee is assisting the NCI in reviewing the Laboratory's mission and planning new initiatives.

Dr. Electra D. Paskett, Marion N. Rowley Professor of Cancer Research, Director, Division of Cancer Prevention and Control, Department of Internal Medicine, College of Medicine, The Ohio State University, conveyed the thoughts resonating in the extramural community that a 19 percent cut on new R01s was equivalent to omitting 1 year of funding from a 5-year award, which could affect completing the specific aims of the project. Dr. Paskett asked whether investigators were allowed to change the scope and/or specific aims of a project after it has been funded and whether the NCI had considered constituting new budget limits for Type 1 applications that realistically reflect the current funding climate as one alternative to the proposed fiscal year 2019 reductions. Dr. Sharpless explained that NCI's R01 award sizes are comparable to those of other ICs and that the FY 2019 cuts to the R01 awards are 2 percent above previous years. The FY 2019 grants are 4-year awards. If the award size of grants starting in FY 2019 is larger than grants ending, the NCI would need to add dollars to maintain the RPG pool funding levels. The trade-off—funding fewer grants and establishing lower paylines—also is challenging. Dr. Sharpless articulated that the scientific understanding about cancer the NCI has built over the past few decades has translated into this increased momentum in cancer research and is a trend that he, as NCI Director, would like to see continue.

Dr. Nancy J. Raab-Traub, Professor, Department of Microbiology and Immunology, School of Medicine, Lineberger Comprehensive Cancer Center, The University of North Carolina (UNC) at Chapel Hill, asked about ways to encourage uniform funding across scientific disciplines in the CSR Study Sections. Dr. Sharpless responded that CSR Study Sections rank grants within a certain pool and that it would be difficult to evaluate uniformity across disciplines without invoking scientific importance. NIH data on bibliometrics suggest that research topics, rather than scientific quality, contributed to funding decisions. Dr. Raab-Traub also requested that the NCI Director's Reports be shared with NCI-Designated Cancer Center directors and faculty.

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

Ms. M. K. Holohan, Director, Office of Government and Congressional Relations (OGCR), reported on the new Congress and committee changes, budget and appropriations, and other legislation of interest. Ms. Holohan pointed out that in the 116th Congress, the House has 235 Democrats (D); 197 Republicans (R), and three vacancies. The Senate has 53 Republicans, 45 Democrats, and two Independents. The new Congress established new leadership and committee changes. Rep. Nancy Pelosi (D-CA) is Speaker of the House, Rep. Steny Hoyer (D-MD) is House Majority Leader, and Rep. James Clyburn (D-SC) is House Majority Whip. Rep. Nita Lowey (D-NY) is Chair of the House Appropriations Committee, and Rep. Kay Granger (R-TX) is the ranking member. Ms. Holohan remarked that for the first time both the Appropriations chair and ranking member are women. In addition, Rep. Rosa DeLauro (D-CT) is Chair of House Appropriations Subcommittee on Labor, Health and Human Services, and Education (L-HHS), which allots NCI's appropriations, and Rep. Tom Cole (R-OK) is ranking member. Ms. Holohan pointed out that these legislators are not new to Congress; they have longstanding relationships with each other, and many have vested interest in cancer research, all of which will be advantages to the work ahead.

Aside from the leadership changes, several members are new to the Appropriations Committee and L-HHS Subcommittee, and four members of the 115th Congress are no longer serving. No changes were made to the Senate Appropriations Committee and L-HHS Subcommittee. The NCI hopes that this continuity will retain priorities and interest in childhood cancer, disparities research, and electronic cigarettes. Ms. Holohan called attention to the leadership of the committees that authorize NIH funding—the House Energy and Commerce Committee and Health Subcommittee and the Senate Health, Education, Labor and Pensions Committee. These committees authorize the NIH annual appropriations to fund specific programs, which may have specific directions attached. In 2018, Dr. Sharpless testified at hearings for both committees.

Ms. Holohan reminded NCAB members that the NCI is funded for FY 2019. On September 28, 2018, the FY 2019 Defense and FY 2019 Labor-HHS spending bill was signed into law, which includes a \$2 B increase for the NIH, a \$79.3 M increase for the NCI, and \$400 M for the Cancer MoonshotSM. Five of the 12 spending bills that together fund 75 percent of the government have been enacted, and seven are incomplete. This led to the record 35-day government shutdown from December 21, 2018, to January 25, 2019, the longest shutdown in American history. The unfunded agencies began operating under a continuing resolution set to expire on February 16, 2019.

Ms. Holohan explained that the release of the President's proposed FY 2020 budget would have been the first step of the NCI/NIH budget process for the regular appropriations, but the government shutdown delayed the budget process because the White House Office of Management and Budget was among the agencies not funded. The OGCR/NCI anticipates that the FY 2020 budget will be released in March 2019, but it may be an abbreviated version. Ms. Holohan noted some complicating matters regarding the FY 2020 budget: The debt ceiling will be reinstated in March 2019, and the budget caps (defense and non-defense) will return on October 2019. Congress will need to either decide on new budget cap levels for discretionary and nondiscretionary accounts or pass legislation to extend the deadlines.

Ms. Holohan noted other legislation of interest to the NCI. The Childhood Cancer STAR Act, which specifies further research efforts in pediatric cancer survivorship and biospecimen collection, was signed into law in June 2018. The recently approved request for applications—Improving Outcomes for Pediatric, Adolescent and Young Adult Cancer Survivors—released in January 2019 aligns with the STAR Act. A spring 2019 virtual meeting is planned, and NCI Program staff will discuss some aspects of implementation.

V. ANNUAL DELEGATIONS OF AUTHORITY—DR. PAULETTE S. GRAY

Dr. Paulette S. Gray, Director, DEA, requested concurrence by the NCAB on two Delegations of Authority to the Director of the NCI. She described the delegations and the provisions in the Statement of Understanding. Delegation A allows the Director to obtain the services of not more than 151 special experts or consultants who have scientific or professional qualifications. Dr. Gray also said that Delegation B specifies that the NCAB delegates authority to the NCI Director to appoint one or more advisory committees composed of private citizens and officials of Federal, state, and local governments to advise the Director with respect to his or her functions.

The Statement of Understanding with NCI Staff on Operating Principles in Extramural Grants also falls within the Delegations of Authority to the Director, NCI. NCAB operations are conducted in accordance with management and review procedures described in the NIH Manual Issuance 4513. Concurrence of the NCAB with recommendations of initial review groups will be required, except for the following: (1) Training grants and fellowships and other non-research grant applications are not subject to NCAB review and approval and, without other concerns, may be awarded without presentation to the NCAB for concurrence, with the exception of Ruth L. Kirschstein National Research Service Awards. (2) Applications over the 20th percentile will not have summary statements presented to the NCAB unless the Institute is considering an award of such an application or other special consideration is requested or required by NCI or NIH policy or for special consideration by an appointed member of the Board. (3) For applications assigned raw scores that are not percentiled, the cutoff will be a priority impact score of 50 for all mechanisms except R41, R42, R43, and R44 awards; for the latter, all scored applications will be included.

Expedited Concurrence: (1) For R01 and R21 applications with percentiled or raw scores that fall within the NCI paylines for that mechanism, a process of expedited concurrence will be used; and (2) the Executive Secretary will alert Board members with responsibility for expedited concurrence when review outcomes for eligible applications are available on the Electronic Expedited Concurrence portion of the Electronic Council Book.

Administrative Adjustments: (1) Permission is delegated to the Director, NCI, to allow staff to negotiate appropriate adjustments in dollars or other terms and conditions of grant and cooperative agreement awards. (2) Administrative requests for increases in direct costs that are the result of marked expansion or significant change in the scientific content of a program after formal peer review will be referred to the Board for advice and recommendation. (3) Actions not requiring Board review or advice—such as change of institution, change of principal investigator (PI), phase-out of interim support, or additional support—need not be reported to the Board. (4) NCI staff may restore requested time and support that were deleted by the initial review group when justified by the PI in an appeal letter or when restoration is in the best interest of the NCI and the project is of high NCI programmatic relevance.

To continue responsible stewardship of public funds, the NIH has instituted a policy of Special Council Review (SCR) of applications from well-funded investigators. Applications from PIs who have \$1 M or more in direct costs from active NIH RPGs must be given additional consideration.

Questions and Answers

Dr. Ley sought clarity on the SCR review of applications \$1 million or more in direct costs. Dr. Gray clarified that the \$1 million in direct costs in RPG awards is annual costs.

Motion. A motion to approve the NCI Annual Delegations of Authority was approved unanimously.

VI. TRIENNIAL INCLUSION REVIEW OF INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH—DR. MARGARET MOONEY

Dr. Margaret “Meg” Mooney, Chief, Clinical Investigations Branch, CTEP, Division of Cancer Treatment and Diagnosis, explained that the NIH policy on the inclusion of women and minorities in all clinical research studies was mandated by Congress in 1993 (P.L. 103-43), in support of the ethical principle of justice and of the importance of balancing research burdens and benefits. Dr. Mooney stated that P.L. 103-43 requires that women and minorities be included in all clinical research studies, including Phase III clinical trials, and that cost is not allowed as an acceptable reason for exclusion. The trial must be designed to permit valid analysis and, for the purpose of the NIH policy, valid analysis refers to an unbiased assessment analysis that does not require high statistical power and should be conducted for both small and large clinical research studies. The 21st Century Cures Act, P.L. 114-255, *Section 2032*, enacted on October 13, 2016, requires the preparation of triennial reports that describe the NIH ICs’ compliance with this requirement. The NIH Office of Extramural Research centrally prepares a summary report, which includes a statement on NCI implementation procedures for the policy, the results, and details on compliance that the NCAB reviews.

Dr. Mooney described the process for preparing the report and the role of the NCI DEA in implementing the policy. The DEA coordinates implementation of the NIH Inclusion Policy across the NCI and ensures Institute-wide coordination and communication. An Accrual Working Group consisting of representatives of NCI Divisions involved in clinical research is convened and information, training, and problem solving are made available. NCI Program Officers work with grant applicants to disseminate policy requirements, and extramural staff are kept up to date via trans-NIH education programs and desktop distribution of policies and procedures.

Dr. Mooney detailed the NCI’s implementation procedures. During the pre-award phase of the grant application process, peer reviewers receive instructions and evaluate inclusion plans for all applications. Where concerns are noted, bars can be made to the award and are put in place. NCI staff work with applicants to ensure appropriate revisions are made. Applications with bars are identified in a closed NCAB session, and a subsequent resolution is reported. During the post-award phase, awardees report cumulative accrual annually, with Program Directors reviewing progress of studies and cumulative accruals. This information is entered into the NIH Inclusion Monitoring System. Staff provides oversight, advice, and assistance and works with awardees to disseminate findings and encourage new studies. The NCI is required to aggregate these data, whether the clinical trial is a treatment or behavioral trial or an epidemiological observation trial. Per the U.S. Public Health Service grant application form 398 instructions, the inclusion of women and minorities sections must include subject selection criteria and rationale, rationale for any exclusions, enrollment dates (start and end), outreach plans for recruitment, and proposed composition using tables. Data on accrual to NCI clinical trials include epidemiological, population-based intervention, and therapeutic trials, as well as subset analyses by race, ethnicity, and sex/gender for all Phase III clinical trials with initial funding after 1995. The current report cycle covers data reported in FY 2016–2018 and was compared with the U.S. cancer incidence for all cancers from FY 2011–2015.

NCAB members were informed about overall reporting data, including specific data for cancer treatment trials. In NCI extramural research studies, enrollment data by sex/gender show a higher percentage of women enrolled than men, a trend similar to previous biennial reports. Excluding all-female and all-male studies (e.g., gender-specific), enrollment data show a relative balance of gender, which aligns with the U.S. cancer incidence. Enrollment data by race/ethnicity also align with the U.S. cancer incidence and show highest minority accrual of Asian and African American populations, with a little underrepresentation of the Hispanic population. Similar enrollment data trends were observed in NCI extramural Phase III research studies. In NCI intramural research studies, which are natural history and

large observational cohorts, the enrollment data varied from 2016 to 2018 regarding race/ethnicity and were comparable with the U.S. cancer incidence.

Dr. Mooney described the reporting data by three NCI programs: CTEP, DCP, and the Division of Cancer Control and Population Sciences (DCCPS). Enrollment data for CTEP treatment trials by race/ethnicity show a cancer incidence rate that matches the U.S. population. In CTEP enrollment data by sex/gender, a higher percentage of women were enrolled for 2 years of the 3-year period; excluding gender-specific studies, the enrollment rates were similar. For the DCP—which represents prevention, screening, and surveillance trials, as well as cancer control studies—trial data by race/ethnicity show a cancer incidence rate that matches the U.S. African American and Hispanic populations, but it varied from year to year. Enrollment data by sex/gender show a higher percentage of women enrolled than men; excluding gender-specific studies, the enrollment rates were similar. The DCCPS accrual to large epidemiologic studies by sex/gender show higher enrollment of men in 2016 and 2017 and higher enrollment of women in 2018. Enrollment data by race/ethnicity, excluding the large epidemiological study conducted in China in 2016, corresponds to the U.S. cancer incidence. Dr. Mooney acknowledged the Accrual Working Group members and expressed appreciation to DEA staff members Ms. Beth Buschling and Ms. Clarissa Douglass for preparing the presentation and answering questions about the report.

Questions and Answers

Dr. Francis Ali-Osman, Margaret Harris and David Silverman Distinguished Professor of Neuro-Oncology Research, Professor of Surgery, Professor of Pathology, Department of Surgery and Pathology, Duke University Medical Center, wondered whether this would be an appropriate time to extend the congressional mandate to include NCI translational data, which is the direction of future clinical trials. Without a mandate, these data on minority representation likely would be skewed. Dr. Gray explained that the NCI is following the mandate as it was issued to the NIH and could not modify the mandate independently. The NIH would need to interact with Congress on any proposed changes to include translational data. Dr. Mack Roach III, Professor of Radiation Oncology and Urology, Director, Particle Therapy Research Program and Outreach, Department of Radiation Oncology, University of California, San Francisco, Helen Diller Family Comprehensive Cancer Center, added that NCI clinical research investigators conducting large-scale trials that are evaluated by CTEP incorporate a translational research component in the study. Audits are built in to review the study minority accrual progress. Dr. Ali-Osman noted the translational studies that are conducted outside of a clinical and suggested that the NIH and NCI could take the opportunity to comment about this topic during any reviews of the existing congressional mandate, *Public Law 103-43*.

NCAB Chair Dr. Elizabeth Jaffee observed that large differences in the 2016 and 2017 enrollment data appeared to be diminished by 2018 and wondered whether these differences could be attributed to a change in the way clinical trials are conducted or trial enrollment. Dr. Mooney replied that it would depend on the study. Large studies, which may have less diversity in minority populations, can influence the results. Efforts are ongoing in CTEP, DCP, and DCCPS to ensure that each trial is diversified compared with the incidence of a particular cancer.

Dr. Paskett sought clarity on the DCCPS 4.7 M unknown/not reported cases from 2016 that were classified as Asian in 2017 and as having enrolled in 2017. Dr. Mooney clarified that the 4.7 M were aggregate cumulative accruals of a trial conducted in China and not newly enrolled patients. Cumulative annual reporting is made for trials that are open. Dr. Paskett also commented on the importance of paying close attention to the unknown/not reported cases and ensuring that the percentage of remains low.

Motion. A motion to accept the report of the Triennial Review of Inclusion of Women and Minorities in Clinical Research was approved unanimously.

VII. NCAB WORKING GROUP REPORT ON THE NCI SMALL BUSINESS INNOVATION RESEARCH (SBIR) PROGRAM—DRS. MEL BILLINGSLEY AND ELIZABETH M. JAFFEE

Dr. Mel Billingsley, President and Chief Executive Officer, Life Science Greenhouse of Central Pennsylvania, and Professor of Pharmacology, Penn State College of Medicine, presented the NCAB *ad hoc* Working Group on SBIR/Small Business Technology Transfer Research (STTR) Working Group Final Report on the NCI SBIR Program. Dr. Billingsley described the SBIR and provided an overview of the NCI SBIR program. Initiated by Congress in 1982, the SBIR is a congressionally mandated set-aside program. The goals are to stimulate technological innovation, increase private-sector commercialization and small business participation in federally funded research, and foster participations by minorities and socially and geographically disadvantaged companies in the technological innovation. Any federal agency with research funding greater than \$1 B also operates a Small Business Technology Transfer Research (STTR) program, with a smaller set-aside than SBIR. The NIH combined SBIR/STTR budget for FY 2019 is \$1.1 B and \$173 M for the NCI.

The NCI SBIR/STTR program structure is divided into phases. Phase I, a feasibility and proof-of-concept study, provides up to \$300,000 for 6–12 months, and applications are received through the NIH Omnibus Solicitation for SBIR and STTR grant mechanism. Phase II provides \$2 M over 2 years and requires both research and development (R&D) and commercialization plans. The projects must relate to cancer therapeutics, diagnostics, cancer devices and imaging, or cancer health information technology. This bench-to-bedside intermediate phase can be labor and capital intensive, and such activities as technology validation and clinical translation are U.S. Food and Drug Administration (FDA) regulated. In 2009, the NCI SBIR program established the Phase IIB Bridge Award, which currently provides up to \$4 M to support previously funded Phase II small businesses in these activities. The expectation is that applicants will secure substantial third-party investor funds (i.e., matching funds) to leverage the NCI investment. Phase III, the commercialization phase, establishes a public-private partnership using non-SBIR/STTR funds. To date, the NCI SBIR/STTR portfolio consists of approximately 475 projects; 89 percent grants and 11 percent targeted and solicited contracts. Therapeutics, the largest sector of awarded projects, compose 43 percent of the portfolio. Dr. Billingsley noted that the NCI has an SBIR Development Center, which sets it apart from some other ICs. The Development Center offers specific programs to enhance businesses' chances of application success, and awardees' likelihood of translational research outcomes.

The Working Group met for a face-to-face meeting at the NCI on May 29, 2018, and was chaired by Dr. Sharpless to evaluate the NCI SBIR program in eight areas—Peer Review, Award Sizes, Portfolio Investments by Areas, Diversity, Resources/Services for SBIR Companies, Resources/Services for Academics, Integrating with Other Programs at the NCI, and Metrics—with eight basic guiding questions to consider. Dr. Billingsley acknowledged the Working Group, which comprises two co-chairs and 11 members representing academia and industry. The Working Group organized in teams to address each of the eight key areas and questions over a series of teleconference calls. In the overall assessment of the NCI SBIR/STTR Program, the Working Group identified several strengths. The SBIR/STTR programs effectively support the mission of the NCI and have both strong centralized management and good flexibility. A high percentage of projects have funded the development of new treatment options. Private investments and company acquisitions significantly leverage NIH investments. The grants process is highly competitive, with success rates of 10–15 percent for Phase I grants and 20–25 percent for Phase II. The rigorous peer review and SBIR/STTR funding substantially reduced the risk of developing early-stage technology. Finally, evidence exists that successful SBIR/STTR grantees have a significant impact on reducing the burden of cancer.

Dr. Billingsley summarized the Working Group recommendations. He emphasized that all recommendations are of equal importance and they are not ordered in the report according to priority.

(1) **Optimizing the review process.** Prioritize the NIH Peer Review Committee's recommendations. Reduce receipt-to-award time to 7 months. Reduce time-to-award for SBIR contracts to 9 months.

(2) **Award sizes and (3) Portfolio balance.** Create a new SBIR Concept grant. Use Administrative Supplements to help Phase I awardees reach value-creating milestones. Increase the Phase I award size to \$400,000.

(4) **Diversity within the portfolio.** Implement a diversity survey at the time of award. Increase women and minority participation on review boards. The Working Group developed a diversity survey that it recommends giving to businesses at the time of award so that the NCI can collect demographic metrics on awardee business leadership.

(5) **Assistance programs.** Initiate an FDA regulatory assistance program. Establish a peer-to-peer mentoring program. An FDA-regulatory assistance program would educate Phase I awardees on the regulatory environment. This program would be web-based, interactive, and scalable. A peer-to-peer mentoring program would enable past SBIR recipients to provide valuable insight to prospective applicants.

(6) **Engaging academic colleagues.** Connect academic investigators with SBIR/STTR. Create a portfolio of resources for academic technology transfer offices. The Working Group encouraged entrepreneur engagement with the NCI-funded Cancer Centers.

(7) **Partnership with other NIH and NCI programs.** Establish a postdoctoral training program. Enhance coordination between SBIR and NCI resources (e.g., NCI Experimental Therapeutics [NExT] program and FNLCR).

(8) **Metrics for evaluating the SBIR/STTR program.** Implement an intake survey for awardees. Repeat the Economic Impact Study every 5 years.

Dr. Billingsley expressed appreciation to Co-Chair Dr. Jaffee, Working Group members, and NCI SBIR Development Center staff for their contributions to the final report.

NCI SBIR 2018 Economic Impact Study: Return on Investment. Dr. Billingsley reported findings of the economic impact analysis (e.g., program evaluation) of the NCI SBIR Program, which was conducted by Montana State University/U.S. Department of Defense TechLink in collaboration with the Bureau Research Division of the Leeds School of Business at the University of Colorado Boulder. The purpose was to evaluate the contribution of the NCI SBIR/STTR program to the U.S. economy and determine key patient and societal impacts resulting from funded technologies. The study evaluated Phase II grants awarded from 1998 to 2010 using the well-validated economic model IMPLAN (Impact Analysis for Planning). During the study period, the NCI invested \$787 M in 444 companies and awarded 690 grants. The analysis showed that 247 products were commercially available, \$9.1 B in sales with SBIR/STTR-funded technologies were achieved, and the average sale was \$13.3 M. The grants generated 107,918 new U.S. jobs and \$2.93 B in tax revenue and added \$26.1 B to the U.S. economy. The response rate for the impact study was high, and data were collected on 91 percent of the companies contacted. The high response rate can be attributed to an official letter from the NCI SBIR Director, a concise survey design, and the persistence of the researchers.

Dr. Billingsley highlighted two examples of NCI SBIR-funded companies. Illumina, Inc. received an SBIR award to develop the Infinium genotyping probe technologies, which currently are used by major online DNA information/DNA privacy sites (e.g., Ancestry and 23andMe), basic and clinical researchers, and the agriculture industry. The Infinium technology led to \$3.5 billion in sales for the company. The

principal investigator for the Infinium SBIR expressed that the NCI SBIR was necessary to develop this technology in its early stages. The second company, Naviscan, now owns three NCI SBIR-funded breast cancer imaging technologies through corporate acquisition. Naviscan's awards, funded between 2003 and 2011, include a high-resolution breast scanner, a biopsy navigator system, and a molecular breast imaging system.

Dr. Billingsley elaborated on the patient benefits resulting from the NCI SBIR/STTR-funded technologies. The study data revealed that from 1998 to 2010, SBIR-funded technologies led to 71 FDA-approved products. An additional 127 products are still in pre-FDA development, and 263 products failed before or during clinical testing. The approved products treat many forms of cancer although attribution of drugs can take many forms after a product is developed and involves confidentiality agreements. Dr. Billingsley attention to one such product, ADCETRIS[®] (Seattle Genetics), one of the first antibody drug–conjugated monoclonals for Hodgkin's lymphoma and large T-cell lymphoma. The fundamental technology used to link the toxin to the monoclonal, which has been applied to several products, was developed using an SBIR grant. Similarly, AZEDRA (Progenics Pharmaceuticals), another drug that was developed on SBIR funding, is a radiopharmaceutical used to treat a rare form of adrenal cancer in a very small pediatric population. In addition, the majority of companies surveyed asserted that the NCI SBIR/STTR funding provided treatment options for a subgroup of cancer patients who previously had lacked options. Companies also indicated that the funding led to fewer invasive treatments or procedures, shortened hospitalization times, and reduced follow-up visits, among other positive results for patients. The full report of the NCI SBIR 2018 Economic Impact Study can be accessed on the NCI website (<https://sbir.cancer.gov/node/685>). Dr. Billingsley expressed appreciation to the NCI for establishing the *ad hoc* Working Group on SBIR/STTR.

Questions and Answers

Dr. Wicha asked how the study data are being used and communicated to Congress. He inquired about the receptivity of Congress to the positive business results of the SBIR program. Dr. Billingsley confirmed that as of February 13, 2019, the Economic Impact Study data are publicly available for stakeholders to use as needed, including for legislative discussion. Dr. Billingsley pointed out that this study was the first time that an NIH IC used the IMPLAN model to assess economic outcomes.

Dr. Sharpless commented that this study illustrates the significant strength of NCI's SBIR program and serves as a communication opportunity for the NCI. The NCI will notify relevant stakeholders about the principal findings of the Working Group Report. Dr. Sharpless explained that the SBIR program is funded through mandated Congressional spending, 3.65 percent of NCI's extramural budget, and that the SBIR program is very popular among members of Congress. Congress understands that biomedical research leads to commercialization activities, and this study provides clear evidence.

Dr. Peter C. Adamson, Chair, Children's Oncology Group and Alan R. Cohen Endowed Chair in Pediatrics, The Children's Hospital of Philadelphia, University of Pennsylvania, asked if there had been any discussion on how to better leverage the program for childhood cancers and therapeutic development. Dr. Billingsley pointed out that the contracting program is the NCI's main leverage to select targets, whereas the omnibus award applicant pool is dictated by market forces. Dr. Billingsley emphasized that the SBIR program should target research areas that do not currently garner significant support. Dr. Sharpless agreed that SBIR can use contracts to address targeted funding opportunities that represent emerging areas of research, including pediatric cancers.

Dr. Charles L. Sawyers, Chairman, Human Oncology and Pathogenesis Program, Memorial Sloan Kettering Cancer Center; Investigator, Howard Hughes Medical Institute; and Professor of Medicine, Weill Cornell Medical College, wondered how many successful SBIR awards depended on an R01 or other grant to produce discoveries that led to the SBIR. Dr. Billingsley referred to a 2018 report soon to

be published in the March issue of the *Proceedings of the National Academy of Sciences* showing that NIH research funding contributed to the discovery, approval, or commercialization of all 210 new drugs approved by the FDA between 2000 and 2016. Dr. Sharpless added that most of the successful SBIR-funded companies often received other NIH funding prior to the SBIR grant.

Motion. A motion to accept the NCAB Working Group Report on the NCI SBIR program was approved unanimously.

VIII. ADJOURNMENT OF OPEN SESSION—DR. ELIZABETH M. JAFFEE

Dr. Jaffee adjourned the open session. Only Board members and designated NCI staff remained for the closed session.

IX. CLOSED SESSION—DR. ELIZABETH M. JAFFEE

“This portion of the meeting was closed to the public in accordance with the provisions set forth in Sections 552b(c) (4) 552b(c) (6), Title 5 U.S. code and 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. appendix 2).”

There was a review of grants and a discussion of personnel and proprietary issues. Members absented themselves from the meeting during discussions for which there was potential conflict of interest, real or apparent.

The Board was informed that a comprehensive listing of all grant applications to be included in the **en bloc** vote was in the Special Actions package. Those grant applications, as well as those announced during the closed session, could be considered for funding by the Institute.

The NCAB **en bloc** motion to concur with IRG recommendations was unanimously approved. During the closed session, a total of 2,635 NCI applications were reviewed requesting direct cost support of \$922,049,873 and 2 FDA applications requesting direct cost support of \$554,710.

X. ADJOURNMENT—DR. ELIZABETH M. JAFFEE

Dr. Jaffee thanked all the Board members, as well as the visitors and observers, for attending.

There being no further business, the 10th virtual meeting of the NCAB was adjourned at 4:19 p.m. on Tuesday, February 12, 2019.

Date

Elizabeth M. Jaffee, Ph.D., Chair

Date

Paulette S. Gray, Ph.D., Executive Secretary