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

1st VIRTUAL JOINT MEETING
of the
BOARD OF SCIENTIFIC ADVISORS AND
NATIONAL CANCER ADVISORY BOARD

Summary of Meeting
April 9, 2020

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

BOARD OF SCIENTIFIC ADVISORS and
NATIONAL CANCER ADVISORY BOARD JOINT MEETING
BETHESDA, MARYLAND
Summary of Meeting
9 April 2020

The Board of Scientific Advisors (BSA) of the National Cancer Institute (NCI) and the National Cancer Advisory Board (NCAB) convened for the 1st Virtual Joint Meeting on 9 April 2020. The meeting was open to the public on Thursday, 9 April 2020, from 1:00 p.m. to 3:15 p.m. and closed to the public on Thursday, 9 April 2020, from 3:15 p.m. to 4:00 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.

BSA Members

Dr. Dafna Bar-Sagi (Chair)
Dr. Kenneth C. Anderson
Dr. Michael John Becich
Dr. Mary C. Beckerle
Dr. Melissa L. Bondy
Dr. Otis W. Brawley
Dr. Graham A. Colditz
Dr. Christopher M. Counter
Dr. Carol E. Ferrans
Dr. Keith T. Flaherty (absent)
Dr. Karen E. Knudsen
Dr. James V. Lacey, Jr.
Dr. Michelle M. Le Beau
Dr. Sylvia Katina Plevritis
Dr. W. Kimryn Rathmell
Dr. Leslie L. Robison
Dr. Martine F. (Sheer) Roussel
Dr. Robert D. Schreiber
Dr. Victoria L. Seewaldt
Dr. Kevin M. Shannon
Dr. David Sidransky
Dr. Ian M. Thompson, Jr.
Dr. David A. Tuveson
Dr. Robert H. Vonderheide
Dr. Eileen P. White
Dr. Cheryl L. Willman

NCAB Members

Dr. Elizabeth M. Jaffee (Chair)
Dr. Peter C. Adamson
Dr. Francis Ali-Osman
Dr. Anna D. Barker* (absent)
Dr. Deborah Watkins Bruner
Dr. Yuan Chang
Dr. David C. Christiani
Dr. Howard J. Fingert* (absent)
Dr. Judy E. Garber
Mr. Lawrence O. Gostin
Dr. Andrea A. Hayes-Jordan* (absent)
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. Susan Thomas Vadaparampil* (absent)
Dr. Max S. Wicha

*Pending Appointments

Alternate *Ex Officio* NCAB Members

Dr. Robert T. Anderson, DOE (absent)
Dr. Michael A. Babich, CPSC (absent)
Dr. Vincent J. Cogliano, EPA (absent)
Dr. Michael Kelley, VA (absent)
Dr. Aubrey Miller, NIEHS (absent)
Dr. Richard Pazdur, FDA (absent)
Dr. Craig D. Shriver, DoD (absent)
Dr. Kerry Souza, NIOSH (absent)
Dr. Lawrence A. Tabak, NIH (absent)

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. Oliver Bogler, Director, Center for Cancer Training
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
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, Director, Division of Cancer Biology
Mr. Peter Garrett, Director, Office of Communications and Public Liaison
Dr. Satish Gopal, Director, Center for Global Health
Dr. Paulette S. Gray, Director, Division of Extramural Activities
Dr. Ed Harlow, Special Advisor to the NCI Director
Dr. Toby T. Hecht, Deputy Director, Division of Cancer Treatment and Diagnosis
Dr. Sara Hook, Director, Office of Scientific Operations, NCI Campus at Frederick
Dr. Tony Kerlavage, Director, Center for Biomedical Informatics and Information Technology
Dr. Douglas R. Lowy, Principal 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. Margaret Mooney, Associate Director, Cancer Therapy Evaluation Program
Dr. Henry Rodriguez, Acting Deputy Director, Center for Strategic Scientific Initiatives
Mr. Jeff Shilling, Chief Information Officer and Chief of Infrastructure and Information Technology Services Branch, Center for Biomedical Informatics and Information Technology
Ms. Donna Siegle, Executive Officer and Deputy Director for Management, Office of the Director
Dr. Dinah Singer, Deputy Director, Science Strategy and Development
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. Deborah M. 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

Liaison Representatives

Ms. Carolyn Aldige, Prevent Cancer Foundation
Dr. Carol Brown, Society of Gynecologic Oncologists
Dr. Margaret Foti, American Association for Cancer Research
Dr. Leo Giambarresi, American Urological Association
Dr. Francis Giardiello, American Gastroenterological Association
Dr. Mary Gullatte, Oncology Nursing Society

Dr. Ruth Hoffman, American Childhood Cancer Organization
Dr. Steven L. Klein, National Science Foundation
Ms. Laura Levit, American Society of Clinical Oncology
Ms. Maria Lopez, Kidney Cancer Association
Dr. W. Marston Linehan, Society of Urologic Oncology
Ms. Margo Michaels, Education Network to Advance Cancer Clinical Trials
Dr. Patricia Mullan, American Association for Cancer Education, Inc.
Ms. Shelly Fuld Nasso, National Cancer Institute, Council of Research Advocates
Ms. Nancy O'Reilly, American College of Obstetricians and Gynecologists
Ms. Leah Ralph, Association of Community Cancer Centers
Ms. Christy Schmidt, American Cancer Society
Ms. Susan Silver, National Coalition for Cancer Survivorship
Ms. Barbara Duffy Stewart, Association of American Cancer Institutes
Dr. Johannes Vieweg, American Urological Association
Dr. Pamela A. Wilcox, American College of Radiology
COL. (Ret.) James E. Williams, Jr., Intercultural Cancer Council

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I. CALL TO ORDER AND OPENING REMARKS—DR. ELIZABETH M. JAFFEE

Dr. Elizabeth M. Jaffee called to order the 1st Virtual Joint Board of Scientific Advisors (BSA) and National Cancer Advisory Board (NCAB) meeting. She welcomed members of the Boards, staff, and guests. Dr. Jaffee expressed appreciation to the NCI leadership for arranging this urgent meeting to update the Boards on national cancer research amid the coronavirus disease 2019 (COVID-19) pandemic. 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 explained the virtual meeting logistics, noting that all microphones will be on mute during the presentations and then unmuted for discussions. Members can ask questions by either the raise-hand or chat features in Webex.

Dr. Gray expressed appreciation to the NCI Center for Biomedical Informatics and Information Technology for setting up the infrastructure for the virtual meeting and the Board members for rearranging their schedules amid the extreme circumstances that the country currently is experiencing.

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

Dr. Norman E. Sharpless, Director, NCI, welcomed members of both the BSA and NCAB to the 1st Virtual Joint Meeting of these Boards. He expressed appreciation to the members for being able to attend this emergency meeting on short notice. Although this meeting will primarily focus on NCI's response to the COVID-19 pandemic, Dr. Sharpless conveyed that NCI's primary focus remains cancer research and care provided to patients by the NCI-Designated Cancer Centers (Cancer Centers). The regular BSA and NCAB meetings on NCI's routine business will continue as previously scheduled. Dr. Sharpless provided an update on NCI's COVID-19 response, legislative activities, and progress in cancer research.

NCI Operations and COVID-19 Response. Dr. Sharpless highlighted the unique capabilities of the NCI and the Frederick National Laboratory for Cancer Research (FNLCR) that are enabling opportunities to respond in such a complex situation as COVID-19. He explained that the pandemic has affected NCI's usual business and mission temporarily; the NCI has adapted and is embracing opportunities to contribute to COVID-19 research. Dr. Sharpless reiterated that cancer research and cancer care remain the leading priority at the NCI. Despite these difficult times, cancer research progress toward the NCI mission of reducing cancer and its adverse effects are being made. The NCI Intramural Research Program (IRP) has a long, decorated history of advancements in virology research. Several NCI scientists and leaders in this field, e.g., Drs. Samuel Broder, Robert C. Gallo, Douglas R. Lowy, John T. Schiller, and Harold E. Varmus, have made landmark contributions to research in human papillomavirus (HPV), human immunodeficiency virus (HIV), and RNA tumor viruses.

The FNLCR, which the NCI sponsors in collaboration with the National Institute of Allergy and Infectious Diseases (NIAID), has unique capabilities and resources that are well suited for an emergency like COVID-19. The FNLCR supports several large-scale projects and national initiatives, including the National Cryo-Electron Microscopy Facility (NCEF) and HPV Serology Laboratory; has unique contracting authorities; and fosters robust collaborative relationships. Lastly, the NCI supports world-class scientists with diverse skills through extramural funding programs (e.g., investigator-initiated grants) via grantee institutions and networks, which have resulted in influential technologies. These scientists have broad reach and skills useful in a pandemic situation.

Because of the COVID-19 pandemic, the NIH and NCI have shifted their in-person day-to-day operations to a remote platform, with staff teleworking to comply with Centers for Disease Control and Prevention (CDC) guidelines on social distancing. Senior leadership meetings are conducted by Webex, and laboratory operations and all nonessential activities are temporarily suspended. The NIH Clinical Center (Clinical Center) remains operational, but the number of elective procedures has been reduced. In addition to treating cancer patients, the Clinical Center is now treating COVID-19 patients with lifesaving therapies. Dr. Sharpless commended the NCI and NIH staff on their ability to reconfigure NCI's 3,000-personnel organization, including contractors, from in-person to remote operations and at such a rapid pace. New cross-government collaborations have been launched rapidly in a direct manner, across both the NIH and the entire federal government.

Dr. Sharpless noted valuable experiences and lessons the NCI has learned from responding to this pandemic and lessons the federal government can capitalize on for doing its best in helping cancer patients and cancer research in the future. In the last few weeks, the NCI has started essential mutual research efforts with other NIH Institutes and Centers (ICs), including the National Institute of Allergy and Infectious Diseases (NIAID); National Institute of Biomedical Imaging and Bioengineering (NIBIB); National Heart, Lung, and Blood Institute (NHLBI); and National Institute on Aging (NIA). The NCI is also working closely with other federal agencies, including the U.S. Food and Drug Administration (FDA), CDC, Biomedical Advanced Research and Development Authority, and other U.S. Department of Health and Human Services (HHS) sister agencies. The first lesson is that telehealth is permanent. In fact, in this important era for population science and implementation of science opportunities, the country has rapidly moved to telehealth, resulting in a significant change in clinical practice and added benefit (i.e., virtual versus in-person visits) to cancer patients. Second, the government can respond quickly in such a time as this and has engaged in complex multi-agency endeavors, all while streamlining processes. In fact, the NCI has designed and opened clinical trials rapidly, which NCI staff will describe later in the meeting.

Dr. Sharpless reported that the NCI is maintaining communications with all stakeholders, including NCI employees, researchers, caregivers, and patients. For people with cancer during the pandemic who are seeking information, the NCI Cancer Information System (CIS) is available by telephone (1-800-4-CANCER), live chat, or email (NCIinfo@nih.gov) and is fully operational, although CIS specialists are teleworking. The CIS receives hundreds of inquiries daily from cancer patients and their families requesting information about being immunocompromised and risks associated with the new coronavirus. Many cancer patients also are receiving responses to their inquiries about visiting their doctors and scheduling critical treatments and diagnostics. The NCI has produced a number of key resources for patients and caregivers to address their concerns about COVID-19. On 13 March 2020, "Coronavirus: What People with Cancer Should Know" was launched. The site has received more than 60,000 visits to date and has become NCI's fourth most visited site. For information specific to NCI grantees, on 25 March 2020, the NCI launched "Coronavirus: Guidance for Cancer Researchers" and has received 1,400 visits. Links to both webpages were provided in the Boards' meeting materials and also can be accessed from the NCI website. Other communications with the research community, internal and external to the NCI, are ongoing, such as virtual town hall meetings, blogs (e.g., NCI Bottom Line), and social media (e.g., Twitter).

Regarding NIH guidance on grants and funding to the extramural community during COVID-19, Dr. Sharpless called attention to the policy updates and guidance documents released by the NIH Office of Extramural Research (OER) addressing funding issues and encouraged the BSA and NCAB members to review these documents. Dr. Sharpless conveyed that the NCI is fully operational and can review grants, disburse funds, and support all related activities. The NCI took questions and concerns from its principal investigators about their grants and suspension of laboratory operations to the OER, which addressed these issues. The following is a summary of the NIH guidance: The NIH has extended

deadlines for the submission of grant applications, with no justification required, and has allowed the use of NIH grant funds for salaries and stipends. Researchers are permitted flexibility concerning project extensions and in accommodating unanticipated costs and extensions of post-award reporting requirements. Numerous flexibilities regarding expenditures of funds are allowed, and extensions for early-stage investigator eligibility due to COVID-19 related disruptions will be considered. The NIH will be flexible with extending time constraints for fellowship, career development, and training awards, including phased awards. Dr. Sharpless noted that any policies the NCI adopts have to align with the policies of the NIH and other grant-making organizations within the federal government.

Legislative Updates. Dr. Sharpless joined Dr. Francis S. Collins, Director, NIH, and other IC Directors to testify at the House Appropriations Subcommittee on Labor, HHS, Education, and Related Agencies (Labor-HHS) hearing on the fiscal year (FY) 2021 NIH budget request on 4 March 2020. The topics included NCI's increase in grant applications, the Childhood Cancer Data Initiative (CCDI), clinical trials, and kidney cancer. The Senate Appropriations Subcommittee on Labor-HHS hearing on the FY 2021 NIH budget request has been postponed until Congress determines the next steps in the appropriations process during the COVID-19 pandemic.

Congress approved three aid packages to address COVID-19 concerning the American economy and patient care and science: Phase 1, Coronavirus Preparedness and Response Supplemental Appropriations Act, enacted 3 March 2020; Phase 2, Families First Coronavirus Response Act, enacted 18 March 2020; and Phase 3, Coronavirus Aid, Relief and Economic Security Act, signed into law 27 March 2020. The Phase 3 coronavirus aid bill includes funding for the NIH, CDC, and FDA; hospitals, health care professionals, and health centers; and provisions for COVID-19 testing for all Americans. Dr. Sharpless explained that the FDA interprets the regulatory authorization on COVID-19 testing to include developing and validating both RT-PCR and serologic analyses. He reiterated the opportunities for making use of the capabilities and resources of the FNLCR in NCI's COVID-19 response.

Progress in Cancer Research. Dr. Sharpless highlighted recent cancer research progress in both intramural and extramural research programs. NCI Center for Cancer Research (CCR) investigator Dr. Nirali Shah, in collaboration with Children's Hospital of Philadelphia investigator Dr. Richard Aplenc, is co-leading the cluster of differentiation (CD) 33 chimeric antigen receptor (CAR) T-cell clinical trial investigating the anti-CD33 CAR-expressing T-cells (CD33 CART) in children and young adults with relapsed/refractory acute myeloid leukemia (AML). The trial has enrolled its first patient. The CAR T-cells used for this first-in-human CD33 CART trial for AML were manufactured in the newly established FNLCR CAR T-cell facility within the Biopharmaceutical Development Program. Dr. Sharpless expressed appreciation to Dr. James H. Doroshow, Deputy Director for Clinical and Translational Research, Director, Division of Cancer Treatment and Diagnosis (DCTD), and FNLCR and DCTD researchers for their efforts in enabling CAR T-cell manufacturing at the NCI-Frederick.

The Division of Cancer Epidemiology and Genetics (DCEG), in a study led by Dr. Charles E. Matthews, Senior Investigator, Metabolic Epidemiology Branch, in collaboration with the NIA and CDC, published findings in the 24 March 2020 issue of the *Journal of the American Medicine Association* that revealed a strong association of daily step count (e.g., steps-per-day), but not step intensity, with a reduction in all-cause mortality rates. Using National Health and Nutrition Examination Survey data, the study specifically showed that U.S. adults with the highest number of steps-per-day had lower all-cause mortality compared with their age-matched counterparts who were less active.

After nearly 30 years of research that began with Dr. Collins, then a faculty member at the University of Michigan, on the discovery that the neurofibromatosis type 1 (NF1) gene is mutated in the congenital pediatric cancer precursor syndrome, plexiform neurofibromas (PN), the first FDA approved treatment, selumetinib, was successfully launched in an NIH clinical trial. Many others in the field,

including a long list of NCI investigators, contributed to this research. Leading those decades-long efforts, Dr. Brigitte C. Widemann, Chief, Pediatric Oncology Branch (POB), CCR, and colleagues in the NCI IRP NF1 program have, over time, developed and optimized a tool, three-dimensional volumetric magnetic resonance imaging for PN, and a therapy of notable success, which they recently published in the 18 March 2020 issue of the *New England Journal of Medicine*. Dr. Sharpless emphasized that although not a cure for NF1, this therapy is meaningful for patients and significantly improves their quality of life.

Dr. Sharpless remarked that the accomplishments in the extramural program are numerous and, in the interest of time, noted one insightful study. The NCI-supported investigator and leading stem cell researcher, Dr. Sean J. Morrison, and his laboratory at The University of Texas Southwestern Medical Center reported a novel relationship between metabolic heterogeneity and the degree of melanoma metastasis in the 18 December 2019 issue of *Nature*. The works of Dr. Morrison and others are helping to address the unsolved complexities of metastatic disease, which will benefit cancer patients in the long term. Dr. Sharpless elaborated on NCI's commitment to the preserve the Research Project Grant (RPG) Pool funding levels, which supports such investigator-initiated research (e.g., R01s, P01s, R21s), and to increase basic science efforts.

Dr. Sharpless announced that Dr. Daniel Gallahan is now Director, Division of Cancer Biology (DCB). He expressed appreciation to Dr. Dinah Singer, Deputy Director, Scientific Strategy and Development, NCI, for her leadership as former Director, DCB.

Questions and Answers

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 (UCSF), Helen Diller Family Comprehensive Cancer Center, inquired about the status of the NCI clinical trials. Dr. Sharpless replied that the pandemic has had significant impact on NCI-supported clinical trials. Accruals have sharply declined, with the exception of trials involving lifesaving therapies for patients who have no other options. The NCI has worked to provide patients flexibility so that they can continue to participate in trials, and the FDA released guidance for clinical trials that allows special circumstances to be considered without the ramification of a protocol deviation. He noted that Dr. Doroshow will provide a detailed report on the NCI clinical trials later in the meeting.

Dr. Jaffee expressed concern about ensuring the careers of new and junior investigators if the pandemic is not resolved soon. Dr. Sharpless pointed out that discussions are ongoing within the NCI on providing early-stage investigators flexibility with their existing awards (e.g., K08 and K99) regarding percent effort for research and training. He encouraged members to review the NCI Bottom Line blog post by Dr. Oliver Bogler, Director, Center for Cancer Training, discussing these issues.

Dr. James V. Lacey, Jr., Director and Professor, Division of Health Analytics, Department of Computational and Quantitative Medicine, Beckman Research Institute, City of Hope, asked about NCI's approach to addressing the disruption in the normal cycle of new trainees coming to the NIH campus and to training centers. Dr. Sharpless explained that the NIH has canceled its summer internship programs for 2020 and pointed out that work (e.g., data analysis or computer science) that does not involve coming to the NIH campus could potentially continue with the associated funding.

Dr. Karen E. Knudsen, Executive Vice President, Oncology Services, Jefferson Health, Enterprise Director, NCI-Designated Sidney Kimmel Cancer Center at Jefferson, Chair and Hilary Koprowski Endowed Professor, Department of Cancer Biology, Director, Thomas Jefferson University, called attention to the Association of American Cancer Institutes (AACI) Slack workspace established as

a platform for AACI members, including Cancer Center directors and NCI leadership, to discuss challenges and share best practices related to cancer care and COVID-19.

Dr. Margaret R. Spitz, Professor, Department of Medicine, Dan L. Duncan Cancer Center, Baylor College of Medicine, expressed concern at the impact of the pandemic on early diagnosis, especially since many of the cancer screening programs have been halted. 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, echoed Dr. Spitz and further elaborated on the long-term effects on colon cancer screening. She also expressed concern about reports of coronavirus shedding in the stool of patients long after the onset of illness. Dr. Lowy emphasized the need to balance the potential benefits against the harms, which resulted in suspending screening for standard of care and research in the short term. Regarding shedding of coronavirus in the stool, Dr. Lowy pointed out that reports published in the 1 April 2020 issue of *Nature* revealed viral RNA in the gastrointestinal tract of nine COVID-19 cases, but infectious virus was not detected.

Dr. Beth Y. Karlan, Vice Chair, Women's Health Research, Professor, Department of Obstetrics and Gynecology, Director, Cancer Population Genetics, Jonsson Comprehensive Cancer Center, David Geffen School of Medicine, University of California, Los Angeles, remarked on an upstaging for new diagnoses because a number of essential cancer surgeries are now elective. Patients are deferring treatments, regardless of their symptoms, which could potentially lead to an increase in mortality rates, primarily because current protocols are less efficient than the standard of care.

Dr. Cheryl L. Willman, The Maurice and Margaret Liberman Distinguished Endowed Chair in Cancer Research, The University of New Mexico (UNM) Distinguished Professor of Pathology, UNM School of Medicine, Director and CEO, UNM Comprehensive Cancer Center, UNM, commented that her institution was able to rotate staff to focus on therapeutic trial accruals because of the challenge to continue screening trials, such as the Tomosynthesis Mammographic Imaging Screening Trial (commonly called TMIST). In addition, patient consent for existing trials has been flexible, and patient contacts for follow-up have been maintained, all of which will help accelerate trial accruals once normal operations resume.

Dr. Mary C. Beckerle, Chief Executive Officer, Huntsman Cancer Institute, Jon M. Huntsman Presidential Endowed Chair, Distinguished Professor of Biology and Oncological Services, Associate Vice President of Cancer Affairs, The University of Utah, asked about plans to expand opportunities in implementation science capitalizing on this unique opportunity of rapid innovation and learning. Dr. Sharpless noted the existing NIH mechanisms focusing on the rapid study of rare events and explained that discussions are ongoing with division directors across the NCI about new implementation science efforts.

III. NCI DEPUTY DIRECTOR'S REPORT—DR. DOUGLAS R. LOWY

Dr. Douglas R. Lowy, Principal Deputy Director, NCI, provided a brief history of the FNLCR, its capabilities, and its role in NCI's response to the pandemic. He also reported on efforts to redirect some of NCI's cancer research activities at FNLCR to research on SARS-CoV-2, the novel coronavirus that causes COVID-19. BSA and NCAB members were reminded that the FNLCR, the only Federally Funded Research and Development Center dedicated to biomedical research, is sponsored by the NCI and is operated by Leidos Biomedical Research, Inc. under the leadership of Dr. Ethan Dmitrovsky. Cancer research performed at the FNLCR, of which the major users are the NCI and NIAID, range from large-scale genomic and proteomic studies, to advanced biomedical computing research. The FNLCR also leads the national oncogenic RAS Initiative, houses two good manufacturing practices (GMP) facilities that produce experimental treatments for first-in-human clinical trials, and operates the NCEF, which is

exclusively used by the extramural community. In addition, NIAID has made extensive use of the FNLCR in responding rapidly to emerging infectious disease epidemics and has supported and led clinical trials in two therapies that proved effective in treating Ebola, including a monoclonal antibody developed and manufactured by the Vaccine Research Center. Recently, NIAID, supported by the FNLCR, opened the Adaptive COVID-19 Treatment Trial (ACTT), a multicenter international trial evaluating remdesivir in hospitalized COVID-19 patients. Remdesivir, a known treatment for Ebola and Marburg viruses, also inhibits replication of coronaviruses. Since February 2020, more than 500 patients have been enrolled in the ACTT, the majority of whom are in the United States.

Dr. Lowy detailed three major SARS-CoV-2 projects supported by the NCI and FNLCR. The Cancer Genomics Research (CGR) Laboratory, DCEG, NCI, is identifying genetic determinants of SARS-CoV-2 susceptibility and outcomes using genome-wide association studies (GWAS). The goals are to (1) rapidly identify variants that can be used as targets for therapy, provide biological insights of COVID-19 pathogenesis, and be used for public health screening and (2) immediately share data with the scientific community. Dr. Lowy emphasized that the COVID-19 pandemic and the HIV epidemic are similar because both have a single etiological agent. The GWAS approach generally yields new insights into diseases of this nature, rather than those as complex as cancer. He also noted that FNLCR investigator Dr. Mary N. Carrington, Director, Basic Science Program, has conducted path-breaking HIV research demonstrating that mutations in the HIV coreceptor/chemokine receptor, CCR5, can decrease the risk of infection. Research in this area has shown the CCR5 mutations can either increase or decrease the risk of infection and rate of disease progression, which has resulted in the development of FDA-approved CCR5 inhibitors. Building on these prior findings and concepts, the CGR has planned three cohort studies in collaboration with NIAID, the Clinical Center, and the National Human Genome Research Institute (NHGRI). The CGR will follow and analyze samples from the Italian epidemic cohort, NIH Clinical Center cohort, and a longitudinal cancer cohort, which Dr. Lowy noted will be further described by Dr. Doroshow later in the meeting.

The FNLCR HPV Serology Laboratory in the Vaccine, Immunity, and Cancer (VIC) Program led by Dr. Ligia A. Pinto is testing and validating serologic assays for SARS-CoV-2. Dr. Lowy explained that this multifaceted laboratory is jointly supported by the Bill and Melinda Gates Foundation and collaborates with the extramural HPV vaccine community, supports NCI vaccine trials (e.g., NCI Costa Rica Vaccine Trial), and leads the HPV Serology Standardization Initiative launched in 2017. Recent data from the VIC Program showed that the GlaxoSmithKline PLC bivalent vaccine Cervarix® induces durable antibody and long-term immunity (e.g., seropositive in the 11-year follow-up) in women receiving one dose. These data have informed a broader HPV vaccine trial in Costa Rica and are providing the basis for converting part of the HPV Serology Laboratory to perform SARS-CoV-2 serology analyses. Multiple laboratories are collaborating in this effort, including facilities at NIAID, CDC, and Mount Sinai Hospital. The short-term goals are to characterize different serologic assays and correlate the data with existing neutralization assays to better understand the possible cross-reactivity interactions from prior exposures to other coronaviruses and to validate serology assays that have been submitted to the FDA for approval. The long-term goals are to improve understanding of the implications of being seropositive in terms of resistance and duration and to participate in the cohort-oriented COVID-19 project described previously.

Using technology developed in the RAS Initiative (e.g., high-throughput tethering screening assays), FNLCR researchers are using high-throughput screening (HTS) for small-molecule inhibitors of SARS-CoV-2 proteins. Dr. Lowy reminded the BSA and NCAB members that the RAS Initiative expanded the RAS-related research of UCSF investigators on using the disulfide tethering approach (e.g., covalent bonding of adjacent cysteine residues) to discover small molecules that directly bind oncogenic mutant forms of KRAS, which is mutated in 30 percent of cancers. This tethering approach to drug design has been widely used in the pharmaceutical industry to develop KRAS inhibitors, which has

led to promising clinical trials, aiming to improve outcomes for these types of cancers. Conceptually, tethering can identify fragment-binding pockets next to cysteine residues, regardless of the protein being studied. The FNLCR's medicinal chemistry group recently has developed and optimized a disulfide tethering library for the RAS project, which also can be used for SARS-CoV-2 HTS. Collaborating on this project are the Department of Energy's Argonne National Laboratory (ANL) and The University of Chicago (UC). Using computational simulations at its supercomputing facilities, the ANL showed that the two SARS-CoV-2 protease targets involved in the viral lifecycle, 3-chymotrypsin-like protease (3CLPro) and papain-like protease (PLPro), have adjacent, exposed cysteine residues that can be targeted and evaluated in FNLCR HTS. In an iterative drug discovery design, the ANL will use artificial intelligence (AI) approaches for identifying therapeutic targets to inform the FNLCR HTS and lead compound identification, which the UC will refine and optimize using medicinal chemistry methods. The ANL next will use AI-based optimization, and the UC will perform *in vitro* inhibition assays against 3CLPro and PLPro and interference assays with SARS-CoV-2. The outcomes will be crystallography of leading compounds and data made publicly available for further research.

Dr. Lowy remarked on how the infrastructure (e.g., design, speed, and flexibility) and expertise of the FNLCR are critical in responding to such a public health threat as COVID-19. He further elaborated on the overall goal of NCI's efforts to partner and collaborate with other research groups and institutions in the global SARS-CoV-2 research to decrease and subsequently subdue the threat of COVID-19 for patients worldwide.

Questions and Answers

Given the pandemic situation and the changes it presents to routine practices, Dr. Jaffee asked how quickly information would be disseminated to the scientific community concerning patients currently being treated to avoid duplicating efforts and how the extramural research groups participating in the SARS-CoV-2 research projects are selected. Dr. Lowy could not provide a specific date when the information would be shared but noted that it would be as soon as possible. He explained that Cancer Center directors overwhelmingly responded to Dr. Sharpless' notification of NCI's interest in performing serology analyses at FNLCR and the need for collecting COVID-19 patient specimens, as well as specimens from patients having prior exposures to coronaviruses in general. Clinical laboratories currently performing SARS-CoV-2 testing are welcome and invited to participate.

In response to a query from Dr. Willman on genetic susceptibility testing and accepting samples from small cohorts in New Mexico with high SARS-CoV-2 infection rates, Dr. Lowy responded that the informed consent process approvals are not completed and noted that the need is great and all samples are welcome, regardless of cohort size. Dr. Stephen Chanock, Director, DCEG, added that CGR is collaborating with NIAID and NHGRI on whole-genome sequencing analyses and, via the CGR omnibus protocol, soon will be allowing the Clinical Center to collect samples. He also called attention to the NIH-wide initiative, one component of which is focused on genetic determinants of SARS-CoV-2, and the international COVID-19 host genetics initiative and accelerated data sharing effort.

Dr. Judy E. Garber, Susan F. Smith Chair, Director, Division of Cancer Genetics and Prevention, Dana–Farber Cancer Institute, Professor of Medicine, Harvard Medical School, asked to what extent the NCI can support the large-scale SARS-CoV-2 projects with FNLCR's budget and whether any funds would be available from other sources in the NIH or from congressional appropriations. Dr. Lowy anticipates that the SARS-CoV-2 research will be funded separately from the regular NCI appropriations, particularly the GWAS, which can be expensive in the long term.

IV. UPDATE: NEW YORK UNIVERSITY (NYU) LANGONE HEALTH CORONAVIRUS ACTIVITY—DR. DAFNA BAR-SAGI

Dr. Dafna Bar-Sagi, Saul J. Farber Professor, Department of Biochemistry and Molecular Pharmacology and Medicine, Executive Vice President and Vice Dean for Science, Chief Scientific Officer, New York University (NYU) Langone Health, NYU School of Medicine, reported on the coronavirus activity at NYU Langone Health system from her perspective as Chief Scientific Officer. She commented that the New York City area became an epicenter for the COVID-19 pandemic quickly and noted that the crisis began for NYU Langone Health when the first patient arrived in the emergency room on 5 March 2020. After Hurricane Sandy, the Langone hospital addressed the issues of management during natural disasters, but those lessons learned were not sufficient to address the COVID-19 challenges. The obvious need was for the capability to respond rapidly to continuously changing demands of unknown scale and complexity.

As an academic center, NYU Langone Health operates across three missions, clinical, research, and education, across three locations, Manhattan, Brooklyn, and Long Island. To address a crisis such as COVID-19, NYU Langone Health first established a workflow to coordinate efforts across the missions and organization. Daily meetings began with the first patient's arrival and included executive and mission leadership from across the organization as well as directors and managers who implemented action items rapidly and effectively. Recognizing that a critical component of the workflow is the data-driven decision-making process, a COVID-19-specific dashboard was developed, updated twice daily, and used to inform prioritizing and executing critical actions. In parallel, multiple settings of communications, including email newsletters, a 24/7 rapid response system, virtual meetings, and an internet portal, were established that had broad reach across the organization to staff, faculty, trainees, and leaders.

Dr. Bar-Sagi detailed three priority areas, genomic epidemiology, clinical trials, and data science, that best describe the early outcomes of the policies implemented and the coordinated efforts in the NYU Langone Health system's response to COVID-19. In the area of genomic epidemiology, testing capacity for COVID-19 was significantly increased, and some flexibility was built into the chain of custody from biospecimens to the clinical laboratory to the biorepository. The NYU Langone Genome Technology Core, in an automated data-generation pipeline, processed up to 400 samples weekly, 250 of which have been sequenced with their data deposited in the Nextstrain open source database. Preliminary real-time SARS-CoV-2 tracking results revealed that the New York City transmission primary came from Europe and that it began mid-February 2020, which was weeks before the first confirmed case. The data also showed novel mutations with potential clinical implications. Dr. Bar-Sagi explained that data are continuously being generated, analyzed, deposited to Nexstrain, and reviewed.

To prioritize research activities, immediately control the spread, and reduce the severity of COVID-19, clinical trials were accelerated and rapidly launched. NYU Langone Health doubled its clinical research operations within 24 hours and added qualified volunteers to the workforce. The clinical research review team processed more than 80 proposals over a 3-week period and activated 32 clinical trials, 30 of which are investigator-initiated and are evaluating multiple therapies, including hydroxychloroquine, convalescent plasma, prophylactic anticoagulants, anti-interleukin 6 (IL-6) clazakizumab, and colchicine. All trials are accruing rapidly, and the clazakizumab trial has been completed. NYU Langone Health is partnering with NIAID on the ACTT and industry on the sarilumab trial.

In a collaborative data science effort, NYU Langone Health researchers and data scientists are integrating machine learning, predictive modeling, and clinical research to address COVID-19 clinical questions to generate actionable plans rapidly. A proof-of-concept study has been completed to assess whether patients with high blood pressure (i.e., hypertension) being treated with angiotensin-converting

enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) are at increased risk for COVID-19. Data from NYU Langone Health electronic health records of 2,765 patients with hypertension were used. The study found no significant correlation between the use of ACE inhibitors or ARBs on the susceptibility of COVID-19 or severity of illness. Recognizing that multiple sources of data are being generated, NYU Langone Health established a secure data-sharing platform,COVID-19 Clinical Data Platform, for these types of data. To date, the consortium consists of more than 20 institutions. Efforts next will focus on expanding on the proof-of-concept study and addressing additional questions.

Dr. Bar-Sagi highlighted that the daily report issued by the New York City Department of Health of new confirmed COVID-19 cases appears to show a decreasing trend, suggesting some degree of control in the crisis. She outlined NYU Langone Health's ideas on key strategies to restarting normal, routine activities and avoiding setbacks: (1) Minimize the risk of disease rebound; (2) Address lost research work and time; (3) Plan for financial challenges on both institutional and societal levels; and (4) Leverage gains enabled by the crisis. She anticipates that these findings will contribute to the national and global initiative to use science to protect people, treat patients, and help restore day-to-day lives across the country.

Questions and Answers

Dr. Martine F. Roussel, St. Jude Children's Research Endowed Chair in Molecular Oncogenesis, Department of Molecular Sciences, The University of Tennessee, Full Member, Department of Tumor Cell Biology, St. Jude Children's Research Hospital, asked about plans to evaluate the combination of anti-IL-6 therapies in the United States similar to the French clinical trial. Dr. Bar-Sagi explained that the NYU Langone Health COVID-19 trials are not investigating such a combination and noted that results from the clazakizumab (anti-IL-6) trial are being reviewed.

Dr. Kevin Shannon, American Cancer Society Research Professor, Auerback Distinguished Professor of Molecular Oncology, Professor, Department of Pediatrics, School of Medicine, UCSF, expressed concern with the financial impact of hiring freezes that many institutions are experiencing and the ramifications to cancer patient care because of COVID-19. He asked whether NCI leadership had plans to discuss this issue with Congress. Dr. Sharpless pointed out that discussions are ongoing in the NCI about the financial aspects and noted that given the significant declines in revenue, appropriators are having discussions about an additional COVID-19 aid package for supporting hospitals in addition to the Phase 3 coronavirus aid bill.

V. CLINICAL TRIAL POLICIES—DR. JAMES H. DOROSHOW

Dr. Doroshow provided an update on the NCI Clinical Trial Network (NCTN) and clinical research activities during the COVID-19 pandemic. He reviewed that 70 percent of cancer patients diagnosed with COVID-19 in hospitals in Wuhan, China, are male; the intensive care unit admission rate is more than 15 percent; and the overall death rate is more than 10 percent. In addition, patients with advanced disease, such as lung, gastrointestinal, and metastatic cancers, are at high risk for COVID-19. Dr. Doroshow expressed appreciation to the health care professionals worldwide for their efforts in maintaining the standard of care for cancer patients (inpatient and outpatient settings) with COVID-19.

Regarding the NCTN trials, Dr. Doroshow reported that from 3 February 2020 to 22 March 2020, the accrual rates across cooperative groups averaged 300 patients weekly, but decreased by 45 to 50 percent beginning 23 March 2020 for all trials (interventional and screening) and across all cooperative groups. A similar pattern is observed in the Experimental Therapeutics Clinical Trials Network (ETCTN) and immunotherapy networks. This decrease is consistent with the fact that many institutions have temporarily closed accruals to most of their studies because of the increased patient

workload for health care professionals to care for COVID-19 patients and the level of care necessary. Despite these challenges, some institutions, including UCSF and the Clinical Center, have continued enrolling patients in trials, particularly for AML and lymphoma studies that offer curative therapies.

Dr. Doroshow detailed NCI's three areas of response to COVID-19 in the NCTN. The NCI is adapting to COVID-19 with modifications to the NCI clinical trial processes. First, Dr. Margaret Mooney, Associate Director, Cancer Therapy Evaluation Program (CTEP), and Dr. Worta McCaskill-Stevens, Chief, Community Oncology and Prevention Trials Research Group, Division of Cancer Prevention, issued memorandums to principal investigators on interim guidance for patients on CTEP-supported and NCI Community Oncology Research Program (NCORP)–supported clinical trials. Per those guidances, patient care can be transferred to different participating study sites. Local health care providers can provide study activities to provide continuity of care, with oversight by the responsible investigator. The NCI can ship oral investigational new drug (IND) agents directly to patients, but injectable CTEP IND agents must be administered at an FDA-registered site. Alternative procedures that do not compromise the safety or integrity of the study will be considered minor deviations. Major deviations may be unavoidable, but must be reported to the central institutional review board (CIRB). On-site auditing visits are being rescheduled; remote auditing has been adopted by NCTN groups. The NCI CIRB supports remote informed consent (e.g., by phone) in conjunction with the patient's signature on written documents.

Second, in the tocilizumab (Genentech, Inc.) compassionate use protocol, the NCI will use its treatment referral mechanism to distribute this IL-6 agent to hospitalized cancer patients with SARS-CoV-2 or severe complications of COVID-19. Dr. Doroshow emphasized that the protocol was developed rapidly by CTEP and POB investigators and explained that negotiations are in progress with Genentech on a study to accrue 200 patients. The eligibility criteria are broad to include patients (over 2 years of age) with severe respiratory compromise from either presumed or proven SARS-CoV-2 infection and intensive care unit patients with or without worsening lung function. The goal is to decrease the amount of time spent in the intensive care unit, on a ventilator, and in the hospital. Investigators will collect limited clinical data and blood samples for biomarker evaluation. The protocol will be activated across the NCTN, but only in institutions not participating in the Genentech-sponsored tocilizumab Phase III trial.

Third, the NCI is building a U.S. national COVID-19 longitudinal cohort of 2,000 patients to support a natural history study at more than 1,000 sites across the NCTN, ETCTN, NCORP, and Cancer Centers in high-, moderate-, and low-prevalence regions. The NCI will fully support per-case reimbursements, ensure that patients from the NCORP Minority/Underserved Community Sites are enrolled, and leverage existing resources (e.g., NCI CIRB) for the study. The governance structure consists of a collaborative extramural/NCI leadership team to oversee a multidisciplinary COVID-19 and Cancer Working Group. The goals are to develop a cohort of cancer patients with SARS-CoV-2 infection/COVID-19 across all age groups and follow a subset of patients for more than l year to assess survivorship and quality of life. Efforts also will focus on the collection of blood samples at study entry and at selected intervals to estimate antibody response and genetic susceptibility and for biomarker development and collection of blood samples from family members. The outcome will be a public database of COVID-19 biospecimens. Dr. Doroshow noted that the COVID-19 and Cancer Working Group has begun its activities and meets daily. The critical milestones are to initiate patient accrual before 15 May 2020, enroll the first 500 patients over a 3-month period after the trial starts, and begin biomarker studies. The aim is to complete patient accruals by 1 December 2020 and complete follow-up and survivorship evaluations by the end of 2021.

Dr. Doroshow described other critical activities related to COVID-19 and clinical trials. More than 12 Cancer Centers have developed COVID-19 therapeutic trials for cancer patients. On 30 March 2020, the Vanderbilt-Ingram Cancer Center established the COVID-19 and Cancer Consortium (CCC-19) with the goal of using a de-identified information, open-access internet database to rapidly

share information to the scientific community. The CCC-19 is now endorsed by more than 70 Cancer Centers, hospital systems, and large clinical practices. In addition, large pharmaceutical companies have sponsored several Phase III trials evaluating IL-6 antibodies and antivirals in both cancer and non-cancer patients with COVID-19.

Questions and Answers

In response to members' queries on the use of biospecimens for assessing COVID-19 risk from cohorts recently completing radiation therapy NCTN trials, changes to patient consent forms, and retrospectively accruing patients for the COVID-19 cohort, Dr. Doroshow noted that similar cohorts have been submitted for supplemental funding for COVID-19 therapeutic trials and explained that consent forms would need to be updated to participate in the new COVID-19 cohort. The initial aim is to establish a prospective cohort, but CTEP has not finalized the eligibility criteria. Members can contact CTEP staff and the NCI coordinator for this study for further details.

Dr. Robert H. Vonderheide, John H. Glick MD Abramson Cancer Center's Professor, Professor of Medicine, Perelman School of Medicine, Director, Abramson Cancer Center, University of Pennsylvania, inquired about the most efficient route to allow Cancer Centers to participate in the national COVID-19 cohort and natural history study. Dr. Doroshow noted that the NCI will promptly notify Cancer Center directors when the study opens and explained that any site that accrues in an NCI-supported trial is eligible.

Dr. Francis Ali-Osman, Margaret Harris and David Silverman Distinguished Professor of Neuro-Oncology, Professor of Neuro-Oncology, Professor Emeritus of Neurosurgery, Duke University Medical Center, asked about specific recommendations for NCI-supported immunotherapy trials and COVID-19 cancer patients. Dr. Doroshow explained that some findings suggest that COVID-19 cancer patients treated with checkpoint inhibitors have worse outcomes, but noted that these data are inconclusive and limited. He anticipates that the COVID-19 natural history study would provide insight into the impact on cancer immunotherapies.

Dr. Sylvia Katina Plevritis, Chair, Department of Biomedical Data Science, Professor, Departments of Biomedical Data Science and Radiology, Stanford University School of Medicine, asked whether such imaging data as chest X-rays and computed tomography scans would be included in the COVID-19 cohort, particularly longitudinally. Dr. Doroshow noted NCI's plan to include imaging data after the study opens in a subsequent amendment and remarked on the interest to also include COVID-19 imaging data in The Cancer Imaging Archive (TCIA).

VI. 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.

VII. NATIONAL CANCER ADVISORY BOARD (NCAB) 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) (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 ongoing intramural research efforts 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.

VIII. ADJOURNMENT—DR. ELIZABETH M. JAFFEE

Dr. Jaffee thanked all of the Board members, as well as all the visitors and observers, for attending. There being no further business, the 1st Virtual Joint Meeting of the BSA and NCAB was adjourned at 4:00 p.m. on Thursday, 9 April 2020.

Date	Dafna Bar-Sagi, Ph.D., Chair, BSA
Date	Elizabeth M. Jaffee, M.D., Chair, NCAB
Date	Paulette S. Gray, Ph.D., Executive Secretary