ACCELERATING THE DEVELOPMENT OF NEW DRUGS AND DIAGNOSTICS

MAXIMIZING THE IMPACT OF THE CURES ACCELERATION NETWORK

Workshop Summary

Steve Olson and Anne B. Claiborne, *Rapporteurs*

Forum on Drug Discovery, Development, and Translation

Board on Health Sciences Policy

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Willing is not enough; we must do."
—Goethe

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This report has been reviewed in draft form by individuals chosen for their diverse perspectives and technical expertise, in accordance with procedures approved by the National Research Council's Report Review Committee. The purpose of this independent review is to provide candid and critical comments that will assist the institution in making its published report as sound as possible and to ensure that the report meets institutional standards for objectivity, evidence, and responsiveness to the study charge. The review comments and draft manuscript remain confidential to protect the integrity of the process. We wish to thank the following individuals for their review of this report:

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Acronyms

AHRQ	Agency for Healthcare Research and Quality
ARPA-E	Advanced Research Projects Agency–Energy
BARDA	Biomedical Advanced Research and Development Authority
CAN	Cures Acceleration Network
CBRN	chemical, biological, radiological, and nuclear
CDC	U.S. Centers for Disease Control and Prevention
CDER	Center for Drug Evaluation and Research
CDRH	Center for Devices and Radiological Health
CIRM	California Institute for Regenerative Medicine
C-Path	Critical Path Institute
CPRIT	Cancer Prevention and Research Institute of Texas
CTSA	Clinical and Translational Science Award
DARPA	Defense Advanced Research Projects Agency
DoD	Department of Defense
DTRA	Defense Threat Reduction Agency
EUA	emergency use authorization
FAR	Federal Acquisition Regulation
FDA	U.S. Food and Drug Administration
FNIH	Foundation for the NIH

IND	Investigational New Drug
IOM	Institute of Medicine
LLS	Leukemia & Lymphoma Society
NCATS	National Center for Advancing Translational Sciences
NCI	National Cancer Institute
NIH	National Institutes of Health
OTA	other transaction authority
PCORI	Patient-Centered Outcomes Research Institute
SBIR	Small Business Innovation Research
STTR	Small Business Technology Transfer
TAP	Therapy Acceleration Program
TIA	Technology Investment Agreement

1

Introduction[1]

Extraordinary opportunities surround the development of new drugs and diagnostics. New technologies and knowledge are creating novel avenues for research and new opportunities for the discovery and clinical development of innovative diagnostics and therapies. Yet, the pathway from basic science to new therapeutics is treacherous. Only a small fraction of investigational new drugs eventually reach the patients who need them. This ever-widening gap between scientific discoveries and the translation of those discoveries into life-changing medications is a major source of frustration for patients, biomedical researchers, businesses, and policy makers.

One response to this gap has been a renewed emphasis on collaborative approaches within federal agencies, academia, and industry directed at the advancement of the drug development enterprise. Among these initiatives is the Cures Acceleration Network (CAN). Originally authorized in the Patient Protection and Affordable Care Act of 2010 (P.L. 111-148), CAN was moved to the newly authorized National Center for Advancing Translational Sciences (NCATS) within the National Institutes of Health (NIH) by the Consolidated Appropriations Act of 2012 (P.L. 112-74). The

[1] The planning committee's role was limited to planning the workshop, and the workshop summary has been prepared by the workshop rapporteurs as a factual summary of what occurred at the workshop. Statements, recommendations, and opinions expressed are those of individual presenters and participants, and are not necessarily endorsed or verified by the Forum or the Institute of Medicine (IOM), and they should not be construed as reflecting any group consensus.

authorizing legislation for CAN requires that it be overseen by a board of 24 diverse members from several fields, including research, the U.S. Food and Drug Administration (FDA), venture capital, and patient advocacy. Though appropriated funding for its initial year was just $10 million, CAN has the potential to catalyze widespread changes in NCATS, NIH, and the drug development ecosystem in general.

On June 4–5, 2012, the Forum on Drug Discovery, Development, and Translation (the Forum) of the Institute of Medicine (IOM) held a workshop in Washington, DC, to explore options and opportunities in the implementation of CAN by NCATS. Entitled "Maximizing the Goals of the Cures Acceleration Network to Accelerate the Development of New Drugs and Diagnostics," the workshop was held in part to respond to congressional interest in CAN expressed in the 2012 appropriations act conference report. The workshop brought together members of federal government agencies, the private sector, academia, and advocacy groups for a day and a half of informative presentations and vigorous discussion. Box 1-1 lists the objectives of the workshop.

This summary of the workshop is meant to inform NCATS, the policy community, patient groups, the public, and other stakeholders as all of these parties work together to enhance the development and testing of therapies and diagnostics. This summary also is being provided to NCATS and to the newly established Cures Acceleration Network Review Board (the CAN Board) to help it identify ways to maximize the impact of CAN and accelerate and expand the availability of cures for patients.

The first chapter of this summary provides an overview of CAN and compiles an overview of the themes of the workshop. Chapter 2 examines different approaches to accelerating translational science, in part through case studies of successful drug development projects. Chapters 3 and 4 examine two unusual features of CAN: the authority to require that some of its grants be matched by funds from other sources, and the authority to use a more flexible form of contracting known as "other transaction authority" (OTA), which has contributed to the success of the Defense Advanced Research Projects Agency (DARPA). Chapter 5 presents perspectives on the role of CAN within the broader drug development ecosystem. Chapter 6 concludes this summary of the workshop with several views expressed by participants of steps CAN could take to have a major impact on the development of cures to improve human health.

THE HISTORY AND GOALS OF CAN

In the first session of the workshop, five speakers discussed the history, organization, and goals of CAN—Tom Insel, Acting Director, NCATS; Sudip Parikh, Vice President of Health Policy, and Managing

BOX 1-1
Statement of Task for the Workshop

This public workshop considered options and opportunities to maximize the usefulness and impact of the CAN program in order to advance translational sciences. The workshop objectives were to

- Identify and catalog potential tools, methods, and approaches that hold promise for accelerating translational science.
  - — Consideration of such promising approaches will draw from the experiences of existing activities at other federal agencies related to the goals of CAN—for example, FDA, the U.S. Centers for Disease Control and Prevention (CDC), and the Agency for Healthcare Research and Quality (AHRQ).
- Discuss the authorities conferred to CAN and identify strategies for effectively using those authorities.
  - — Consideration of the CAN authorities will specifically explore the flexible research, or "other transaction," authority and will reference existing efforts in which such authority is currently applied across other federal agencies—for example, DARPA, the Defense Threat Reduction Agency (DTRA), and the Biomedical Advanced Research and Development Authority (BARDA).
- Explore promising models for public–private collaborations that could be strengthened or facilitated by activities under CAN.
  - — Discuss barriers to such collaborations and identify opportunities and potential solutions for moving past the identified barriers.
  - — Discuss the respective roles of multiple sectors, including, for example, the pharmaceutical and biotechnology industries, venture capital and private equity, and patient advocacy groups.
- Identify barriers and potential solutions to facilitate coordination of activities under CAN with the FDA regulatory review process and timelines.

Director, Centers for Public Health Research and Evaluation, Battelle Memorial Institute; Lili Portilla, Director, Office of Strategic Alliances, NCATS; Barbara McGarey, Deputy Associate General Counsel for Public Health, Office of the General Counsel, NIH; and Kathy Hudson, Acting Deputy Director, NCATS, and Deputy Director for Science, Outreach, and Policy, NIH Office of the Director. The first part of this chapter provides an integrated summary of their remarks. The latter part of the chapter provides an overview of the themes of the workshop identified individually by five speakers during the workshop's final session. It should not be construed as reflecting consensus or endorsement by the planning committee, the Forum, the workshop participants, or the IOM.

The History of CAN[2]

In 2003, when Joe Lieberman was running in the Democratic presidential primary, he called for a $150 billion, 10-year federal initiative to bring cures for diseases quickly to the marketplace. This call contributed to the introduction of both the American Center for Cures Act of 2005, which called for a center within NIH with an authorization of $5 billion, and the similar Accelerating Cures Act of 2008. Neither bill made much progress in Congress, but the ideas contained in the bills caught the attention of Senator Arlen Specter. In 2009, as the recession severely affected the biotechnology industry, Specter began working on legislation designed to magnify the effect that patient advocates were having on the search for cures to disease. Meetings with patient advocates and venture capitalists led to the idea for a Cures Acceleration Network—a name originally suggested by the autism community, according to Parikh.[3] The network was intended to have the following characteristics: authority to give large awards, a program allowing for matching grants to take advantage of the passion and expertise of patient groups, and administration outside NIH. Additional goals were to broaden the range of eligible grantees and reviewers, with the latter including venture capitalists and patients. It would have a competitive prize component and funding authorities like those granted to DARPA.

The Cures Acceleration Network Act introduced by Specter called for an entity outside NIH with a program managed by a high-level board. Independence from NIH was intended to tap into a different culture than the one prevalent at NIH. It would have authorized the use of interagency agreements, with the Center for Scientific Review performing peer review, and it would have prescribed the expertise necessary for members of the initial review group. The act would have increased the authorization for NIH to $40 billion, with $1 billion for CAN.

Many, though not all, components of this legislation were passed in the Patient Protection and Affordable Care Act of 2010. CAN was established in NIH, in the Office of the Director, not as an independent entity. (As discussed below, the program was subsequently moved to NCATS.) It had an authorized budget for fiscal year (FY) 2010 of $500 million. New award mechanisms include Cures Acceleration Partnership Awards of "not more than $15 million per project for the first fiscal year for which the project is funded"; Cures Acceleration Grant Awards of the same size; and Cures

[2] This subsection is based on remarks given by Sudip Parikh, Vice President of Health Policy, and Managing Director, Centers for Public Health Research and Evaluation, Battelle Memorial Institute.

[3] Parikh was at the time a congressional staff member working on the legislation with Senator Specter.

Acceleration Flexible Research Awards with a flexible, or "DARPA-like," funding authority that could represent up to 20 percent of CAN's budget.[4] The 24-member CAN Board was to include patient advocates and venture capitalists and was to advise the NIH director about barriers to successful translation of basic science into clinical applications.

However, CAN would not exist until money was not just authorized, but appropriated for it. According to Parikh, the patient advocacy community provided enormous support for the appropriation, and several influential articles in the media argued for the kind of capacity that would be created by CAN. At the same time, industry was forming innovative partnerships with universities in an effort to create new research and development (R&D) models for the development of drugs and diagnostics.

As part of the Consolidated Appropriations Act of 2012, enacted at the end of 2011, CAN was finally launched (see Appendix B). It was placed within the newly established NCATS, which was established in the same Act for FY 2012 to catalyze the generation of innovative methods and technologies that will enhance the development, testing, and implementation of diagnostics and therapeutics (see Box 1-2). Parikh commented that NCATS, as conceived and structured, offers the culture originally envisioned for CAN—different from, while complementary to, the traditional activities and focus of NIH. The appropriated budget for CAN in FY 2012 was only $10 million.

The Structure of NCATS and CAN

At this level of funding, CAN is the smallest of the four major programs and initiatives within NCATS—Clinical and Translational Science Activities, Rare Diseases Research and Therapeutics, Re-engineering Translational Sciences, and CAN.

As Insel emphasized, most of the translational science being supported by NIH is going on through the 26 institutes and centers other than NCATS. However, those other institutes and centers need NCATS to catalyze the tools that enable the rest of NIH to do things better, faster, and cheaper. There was discussion during the workshop of what Hudson called "cool tools," such as an ongoing partnership with pharmaceutical companies to find new uses for old drugs. NCATS was established in part to support the development of these tools and thereby catalyze projects elsewhere in NIH. Insel also noted that the center's Clinical and Translational Science Award (CTSA) consortium—a national consortium of about

[4] This authority is also known as "other transaction authority" (OTA). See Chapter 4 for further discussion of the "DARPA-like" authority.

60 medical research institutions that accounts for more than 80 percent of NCATS' $576.5 million budget in FY 2012—"has created the potential for a national network that can be the flagship for what we do in translational science at academic sites around the country."

The legislation for CAN authorizes three award programs: the Cures Acceleration Partnership Program, the Cures Acceleration Grant Program, and the Cures Acceleration Flexible Research Program. The legislation also authorizes large grants, not to exceed $15 million per fiscal year. Congress must explicitly appropriate funds for CAN or its programs in order for NIH to fund them, observed McGarey. NIH is specifically prohibited from using any funds from its general appropriation to fund CAN activities. According to McGarey, this is unusual for NIH authorities, though she noted that she did not anticipate it being a problem, "unless, of course, Congress appropriates no money for CAN." Insel also noted that CAN has the potential to work in partnerships with other NIH institutes and centers, including the CTSAs in NCATS, even though funds cannot be transferred into CAN.

The purpose of CAN is to accelerate the development of high need cures through the development of medical products and behavioral thera-

BOX 1-2[a]
The Need for Translational Science

Biomedical research has now revealed the molecular basis of more than 4,000 individual diseases, Insel noted in his introductory remarks. However, only about 250 of these diseases have molecular therapies, and over the past decade only 17 to 34 new molecular entities have become available each year to treat disease. "At that pace, if each [drug] was used for one disease, we would be about where we want to be in a hundred years," said Insel. "This is obviously not workable."

The development of new therapeutics is slow, expensive, and failure-prone. On average, for every 10,000 new compounds discovered, only one becomes a new drug. About 95 percent of drugs fail in clinical trials, with 82 percent dying in Phase 2 alone.

NCATS was created to bring science to bear on the development of drugs and diagnostics. Its focus is on the process and the pipeline to accelerate the pace at which basic research is translated into treatments. For example, it views the drug development process not as a linear path from laboratory to clinic, but as an iterative process in which feedback loops connect basic research, translational research, clinical research, population research, and public health.

[a] This box is based on the presentation by Tom Insel, Acting Director, NCATS.

BOX 1-3[a]
Functions of CAN in Authorizing Legislation

1. Conduct and support revolutionary advances in basic research, translating scientific discoveries from bench to bedside.
2. Award grants and contracts to eligible entities to accelerate the development of high need cures.
3. Provide the resources necessary for government agencies, independent investigators, research organizations, biotechnology companies, academic research institutions, and other entities to develop high need cures.
4. Reduce the barriers between laboratory discoveries and clinical trials for new therapies.
5. Facilitate review in FDA for the high need cures funded by CAN, through activities that may include
   a. the facilitation of regular and ongoing communication with FDA regarding the status of activities conducted under this section;
   b. ensuring that such activities are coordinated with the approval requirements of FDA, with the goal of expediting the development and approval of countermeasures and products; and
   c. connecting interested persons with additional technical assistance made available under section 565 of the Federal Food, Drug, and Cosmetic Act.

[a] See Appendix B.

pies (see Box 1-3). The statute defines both medical products and high need cures very broadly, with a significant amount of discretion to work strategically in the translational science arena. CAN has the typical NIH program authority to conduct or fund both intramural and extramural activities. Also, one of the specifically articulated functions of CAN is to facilitate review by FDA of the research funded by CAN for high need cures. McGarey commented that this is an interesting purpose conferred under statute for an NIH program, which will allow NIH to undertake or fund activities targeted to coordination of research in FDA review.

The CAN Board is to have 24 members appointed by the Secretary of the Department of Health and Human Services.[5] It is to have

[5] The CAN Board composition was announced on August 30, 2012. The members are listed at http://www.ncats.nih.gov/about/org/advisory/can-board/roster/roster.html (accessed August 30, 2012).

- at least one member eminent in each of the following areas: basic research, medicine, biopharmaceuticals, discovery and delivery of medical products, bioinformatics and gene therapy, medical instrumentation, and regulatory review and approval of medical products;
- at least four members recognized as leaders in venture capital or private equity investing; and
- at least eight members representing disease advocacy organizations.

The congressional conference language from the 2012 appropriations bill encourages the CAN Board to create measurable outcomes to track CAN's successes.

Insel noted that advisory boards at NIH have different characteristics at the different institutions and centers. At NCATS, the responsibilities of the CAN Board are to advise and provide recommendations to the Director of NCATS regarding the policies, programs, and procedures for carrying out the duties of the Director and to identify significant barriers to the successful translation of basic science into clinical application, including issues under the purview of other agencies and departments. The CAN Board will provide a second level of review for projects, but, said Insel, it also will provide "a lot of wisdom beyond just those individual projects." The membership of the CAN Board and the NCATS Council will overlap so that there is synergy rather than conflict between their respective scope and responsibilities.

There are mechanisms other than congressional appropriations that could potentially fund CAN activities. For example, NCATS, like all other NIH institutes or centers, can accept gifts, either unconditionally or with strings attached, though offers can be rejected if the conditions are unacceptable. NIH also can work through the Foundation for the NIH (FNIH) to generate ideas for collaborative projects. These projects still need to go through the NIH review process, which can impose delays that are unacceptable to outside collaborators. But NCATS can interact with FNIH not only by raising an idea for funding but also by providing matching funds for an idea, which has not been possible in the past.

Matching Grants and OTA

CAN's authorizing legislation gave it several authorities that are uncommon for government agencies, and for NIH in particular:

- The Cures Acceleration Partnership Awards have a one-to-three matching requirement. The match is waivable by the NCATS Director. (These matching requirements are the subject of Chapter 3.)

- The legislation also provides CAN with the authority to use the full scope of government funding mechanisms, including cooperative agreements, contracts, and OTA. (Chapter 4 explores the features of OTA in detail.) Flexible research awards exercising OTA are limited to 20 percent of the total funds appropriated to CAN in a fiscal year. Also, the NCATS Director must have determined that the goals and objectives of the awards cannot adequately be carried out through conventional contracting agreements.

OTA "is best described as what it is not," said Portilla. It is not a grant, contract, or cooperative R&D agreement. Instead, it provides for greater flexibility in putting together an agreement to get a project done. Congress must explicitly authorize an agency to use OTA to obligate funds. Although NIH has historically had the authority to use OTA, only a single NIH staffperson was trained to work with it, and the authority was little used.

Under OTA, certain government regulations and policies do not necessarily apply, including the Federal Acquisition Regulation (FAR), provisions of the Bayh-Dole Act, and NIH peer-review requirements. This authority thus allows an agency to attract nontraditional partners who would otherwise have concerns about conventional federal regulations and policies. In other agencies that have used OTA, the timelines to getting projects done have been shorter than elsewhere in government. OTA also has the effect of encouraging cost sharing among partners, both public and private.

OTA can eliminate some of the barriers to establishing unique partnerships, said Portilla. However, because each arrangement conducted under OTA is different, so too are the metrics designed to evaluate the success of an agreement. "Up front you are going to have to determine what the metric is that you are trying to measure with each one of these agreements," said Portilla.

Unique Features of CAN

Hudson emphasized several of the features of CAN that collectively set it apart from not only programs of other NIH institutes and centers but from those of other government agencies. The first is that CAN is designed to be *catalytic*, which will be essential given its small initial budget. (The first year of CAN funding is about the same as is authorized for a single award.) Under such circumstances, what is needed, said Hudson,

are ways to "catalyze interesting, novel collaborations, get work done faster, and make a real difference in patients' lives."[6]

A second prominent feature of CAN will be its *collaborative* nature, a feature that it will share with NCATS. Collaborations already under way at NCATS with DARPA, FDA, the pharmaceutical industry, and patient advocates all demonstrate this commitment to partnerships, Hudson said.

Third, both CAN and NCATS are committed to open *communication* and information gathering from the community. "Today's workshop is an example of that," said Hudson. "We are seeking to hear from the community, broadly defined, what are the barriers that are standing in the way of developing new cures and diagnostics and devices, and how can we focus our attention on developing tools that will help speed the development of those drugs."

Finally, NCATS and CAN will be *countercultural*, with a different culture than the rest of NIH. Though as Parikh had explained, CAN was originally meant to be separate from NIH; its placement within NCATS maintains the opportunity for it to have a distinct culture. NCATS represents "a different culture growing inside of NIH," Parikh said. "It complements NIH."

Questions for the Workshop

Insel concluded his talk by raising several questions pertinent to the core mission of CAN for consideration at the workshop:

- How will CAN have the greatest impact?
- What tools, methods, and approaches can accelerate translational science?
- What is the best use of the matching and flexible research authorities established in legislation?
- How will CAN assist public–private partnerships?
- How will CAN interact with the ongoing regulatory science initiative at FDA?

He also emphasized the need for some "early wins" from CAN. "We need to be able to show how this can be used to do something that hasn't been done before."

[6] Parikh also emphasized the potential for CAN's budget to grow. "What you are planting is a seed that over time will grow pretty quickly, especially depending on the submissions that are made by NIH and by the White House. It may be $10 million today. Your post-docs will hopefully have more to work on."

OVERVIEW OF THE THEMES OF THE WORKSHOP

In the final session of the workshop, speakers individually identified the themes that emerged over the course of the workshop. These themes are described here as a way of providing an overview of the major topics discussed at the workshop that encapsulate the key issues surrounding the creation of CAN and its future course.

Approaches to Accelerating Translational Science[7]

CAN does not yet have the funding to support major projects, but it can be a crucial catalyst for innovation within NCATS. To do so, Bill Chin, Executive Dean for Research, Harvard Medical School, noted that it needs to foster a bidirectional flow of information between basic scientific research and the process of translating scientific results into products. It also needs to create new knowledge through interactions among diverse groups. In particular, barriers to collaboration still exist between the academic and industrial talent pools.

Collaboration can de-risk drug development efforts through public–private partnerships. Many of these efforts will be precompetitive, but at least some could be in the product development space where private-sector competition exists. Chin argued that the traditional technology transfer model in academia needs to be transcended, and more drug discovery and development data need to be shared. The CTSAs could also be a vehicle for training investigators who would then be prepared to collaborate by virtue of their education and experience.

The organization of translational science could enable progress. Collaborative teams of passionate investigators can pursue ambitious goals. Therapeutic discovery could be decentralized, decision making streamlined, bureaucracy reduced, and flexibility enhanced. Planning and project prioritization need to be done on a programmatic, not episodic or grant-by-grant, basis for maximum effect, and effective project management is key. Open-source models of innovation are tremendously exciting. Other novel approaches include crowdsourcing, prizes, or other incentives.

A virtual model of drug discovery could produce important advances. In the area of tools development, CAN could help explore how technology can positively affect the translational process. Key areas of both scientific and technological development cited at the workshop include

- development of better animal models;
- use of stem cells;

[7] This subsection is based on remarks given by Bill Chin, Executive Dean for Research, Harvard Medical School.

- development and promotion of scientific areas such as
  — systems biology,
  — chemical biology,
  — regulatory science, and
  — informatics;
- development of molecular libraries;
- innovation in clinical trial design; and
- improvement of target validation.

Chin cited as a provocative suggestion mentioned at the workshop the development from scratch of a more effective and efficient regulatory process. For example, efforts could focus on creation of a new development and regulatory pathway for more rapid approaches to proof of concept or proof of mechanism in a Phase 1B or 2A. After feasibility assessment, implementation could be undertaken for those aspects of that system that are thought to be feasible.

Matching Authority[8]

As the demands on resources become greater, matching grants offer an opportunity for both collaboration and synergy. They also reduce the risk for partners who are willing to experiment, and successful experiments on a small scale then can be replicated and disseminated. Nancy Sung, Senior Program Officer, Burroughs Wellcome Fund, noted that it is important to get partners engaged with each other early in the process. Through early involvement, partners can shape the project from the start.

Agency support for partnerships can vary from a relatively hands-off approach to active solicitation, management, and support of partnerships. CAN will need to pick a place along this continuum that best takes advantage of the corresponding opportunities. Similarly, partnerships can range from one-on-one interactions to large multistakeholder forums. It will be important to bring partners up to speed, help them understand the context, and forge personal connections.

Training for those who are interested in commercializing discoveries can be extremely valuable. Tailored curricula, mentoring, and webinars are all possible ways of building skills and knowledge. What makes a project attractive to investors? What kind of reproducibility do regulators expect? What kinds of information need to be treated confidentially, and what kinds of information can be freely shared? Widespread understanding of such topics through training strategies can reduce

[8] This subsection is based on remarks given by Nancy Sung, Senior Program Officer, Burroughs Wellcome Fund.

the need for written agreements, especially during the early stages of collaboration.

The risks associated with projects funded by CAN will not be the same as the risks of other NIH projects. Projects will be done not just faster and better, but differently. The risk profile of CAN's portfolio of projects will need to be actively monitored to find the "sweet spot" where risks are taken but also are manageable.

OTA[9]

While OTA has not necessarily been essential to the success of DARPA and other agencies, it is an effective tool for those who have access to it. It allows federal agencies to partner with organizations, and particularly large companies, that have concerns about the standard federal contracting process.

OTA essentially allows a government agency to start with a blank piece of paper in writing a contract with a nongovernmental organization. According to Daniel Wattendorf, Program Manager, Defense Sciences Office, DARPA, success requires that the people who are relevant to the discussion be represented and that they are able to convey to each other what they want to achieve. They also need to discuss issues, such as intellectual property, where there may be concerns and address those concerns at the beginning of a project so that all of the partners to an agreement know what is expected. Staff training and competencies are key elements. A strong relationship between the program manager and the contracting officer has contributed to many of the successes of DARPA. OTA contracts can be more time-consuming to set up at the outset, but they can be easier to execute because everyone understands the terms of the agreements.

Wattendorf noted that a major function of DARPA has been to serve, in essence, as the venture capital arm of the Department of Defense (DoD), and OTA helps make that role possible. In the same way, the use of OTA could help make CAN and NCATS the venture capital arm of NIH.

Situating CAN Within the Drug Development Ecosystem[10]

The ecosystem for the development of cures is complex and resistant to change, but momentum currently exists to change the system. In particular, patient groups have played an increasingly powerful part in motivating

[9] This subsection is based on remarks given by Daniel Wattendorf, Program Manager, Defense Sciences Office, DARPA.

[10] This subsection is based on remarks given by Margaret Anderson, Executive Director, FasterCures.

and helping to generate new cures. This prominent new role of patient groups will be a major consideration as CAN takes shape.

Public–private partnerships are essential but require time, effort, and communication to succeed, Margaret Anderson, Executive Director, FasterCures, observed. Partnerships are particularly needed where resources are constrained, as is the case with the current funding levels of CAN. However, patient groups have demonstrated that even small amounts of funding, if strategically applied, can have major effects.

To accelerate the development of cures, CAN will need to function differently rather than emulating other government programs. At the same time, it needs to work closely with other agencies, including other parts of NIH and FDA. In particular, CAN and FDA will need to communicate early and often. Officials from FDA have expressed their eagerness to work with CAN because of CAN's potential to help them solve problems they face. This cooperation could be a model for interagency collaboration, and this collaboration could form the basis for much broader changes in the drug development ecosystem.

2

Approaches to Accelerating Translational Science

Key Messages[a]

Promise for Translational Science

- New technologies would help change the translation process in positive ways rather than simply enhancing processes that are already in place.
- Open innovation could decentralize and speed the development of new drugs and diagnostics.

Approaches for CAN

- Partnerships among institutions help accelerate the rate at which new discoveries are translated into products that can improve health. CAN could incentivize, de-risk, and facilitate research at the academia–industry interface.
- CAN could curate features of promising and successful alliances among academic, philanthropic, and industry groups and make available a compilation of the most promising features as guidelines or best practices templates.
- Planning on a programmatic, not episodic, basis will help facilitate overall effectiveness of drug development and the impact of CAN to improve and accelerate development of cures.
- Effectiveness of and communication among the project management team is a key element of success.
- A consensus-based traditional funding review process could undermine support for needed breakthrough projects.

[a] Identified by individual speakers.

CAN is part of a much broader effort in NCATS and NIH to help accelerate the translation of biomedical discoveries into products and processes that improve human health. The second session of the workshop focused on ways to achieve this goal, with an emphasis on exemplary projects that have met with success. Past experience has provided lessons about how to replicate successes and what to avoid. CAN will have the capability to support translational science both through projects aimed at specific diseases and through the development of more generic tools, and the proper balance between these two was discussed throughout the workshop.

CYSTIC FIBROSIS AND THE NEED FOR PARTNERSHIPS[1]

Cystic fibrosis is caused by mutations in the CFTR gene, which encodes a protein that pumps chloride across epithelial cell walls. As a result, mucus gradually plugs the lungs, degrading their function. Cystic fibrosis causes a loss in lung function of about 2 percent a year. Once lung function gets below about 50 percent, severe disability results. When lung function drops below 40 percent, death is likely from one of a variety of causes.

About 15 years ago, Vertex Pharmaceuticals and the Cystic Fibrosis Foundation began working together to lower lung decline to 1 percent per year, said Joshua Boger, who founded Vertex Pharmaceuticals in 1989 and still serves on its board. If that could be achieved, people with cystic fibrosis could live nearly a normal life expectancy. Yet, at the time, that goal seemed out of the realm of a pharmaceutical intervention.

Vertex took two approaches to enhance mutant CFTR function. One was to find small molecules, known as CFTR potentiators, that could increase the channel activity of CFTR protein at the cell surface, resulting in enhanced ion transport. The other was to identify molecules known as CFTR correctors that could increase the quantity of functional CFTR protein at the cell surface, also resulting in enhanced ion transport. In the late 1990s, these goals were generally considered to be science fiction, said Boger, especially given that many patients would need both treatments.

The most important step in making these goals a reality, said Boger, was to create a good assay for the performance of test molecules. "Once we had the right assays, compounds that did exactly what we wanted them to do were relatively easy to find." More than 300,000 compounds were screened, resulting in the identification of several effective compounds, including a drug now known as ivacaftor. Clinical trials dem-

[1] This section, including subsections, is based on the presentation by Joshua Boger, Founder, Vertex Pharmaceuticals.

onstrated that treatment with ivacaftor in patients who have a particular mutation can produce a 10 percent increase in lung function within a matter of weeks. Young patients who struggled to keep their weight up gained weight almost immediately with the drug. And adverse effects were greater in the placebo group than in the treated group because the placebo group was sicker.

Beginning with patient observations in 2008, three Phase 2 trials were held and a New Drug Application was filed in October 2011. Regulators acted with great speed and approved the drug in just over 90 days. The drug development process cannot be done much faster than it was done for ivacaftor, Boger said. "This is a success story in large part due to unique cooperation between Vertex and the Cystic Fibrosis Foundation, which has become a model in the field," said Boger.

Partnerships and Approaches

Until the late 1990s, the Cystic Fibrosis Foundation supported "wonderful science," according to Boger, but the foundation's leadership realized it was not directly helping patients. As a result, leadership shifted the organization's research focus from late in the laboratory to early in the clinic. They also founded the partnership with Vertex, which Boger termed a "very bold idea" that would not have gotten through most review processes in government or disease foundations. Total support for the collaboration from the foundation was about $75 million. This is about the maximum size of the project that CAN could support if appropriations were available, Boger noted.

The development of ivacaftor was a "high-wire act from beginning to end," Boger commented. Success was never obvious or guaranteed. "If you are looking for dramatic changes in medicine, you are not looking to be comfortable in research and development." Such a project would not be possible in most of NIH because, as Boger said, "every breakthrough project that I know about has passionate detractors." A review process that depends on consensus will not support breakthrough projects. He noted that breakthroughs require human passion. "In any sort of multistakeholder project that is being talked about through CAN, think about how you are going to put human passion into it."

He also noted the importance of developing assays that report relevant information. Boger emphasized that assays are different from validated models (which tend not to be aimed at breakthroughs) and from disease models (which may or may not be part of determining how to treat that disease).

Critical Needs for Translational Science

These observations from the example of cystic fibrosis point to several critical needs for translational science, according to Boger. One is for technologies that positively change the translation process, not just add to processes already in place. For example, how can a technology make translation faster, cheaper, or more effective? How can risk be lowered while safety is enhanced? How can technology enable greater leaps? Technologies that are simply more accurate are not sufficient answers to these questions. Technologies need to contribute to systems that replace other systems.

Today, a drug development effort can be shut down with one negative result. Some drugs can be rescued, but even more important is to create a process that eliminates false negatives in the first place. "I am positive that we have fantastic drugs that have been killed in development," said Boger. "False negatives, I believe, are the biggest problem in the drug development process right now."

Cures for the kinds of diseases that are a focus of the CAN legislation also require that a significantly more effective and efficient regulatory system be envisioned "from scratch," said Boger. The current process is built on historical precedent, but, he said, even though regulators do their best, the process is too expensive and too long. Safety, risk, and efficacy assessments need to be conducted on the continuum of both premarket and postmarket, not as an ad hoc, focal point process that evaluates only one drug, one development process, at a time. Boger emphasized that public health and overall societal benefits need to be incorporated into the evaluation process on a routine and continuing basis. Expenditures of time and money need to be optimized, and patients need to receive benefits sooner.

ALZHEIMER'S DISEASE AND THE DRUG DEVELOPMENT ECOSYSTEM[2]

The biomedical enterprise is capable of stunning successes, but it is also falling short of meeting the needs of patients in many ways, said R. Sanders (Sandy) Williams, President, the Gladstone Institutes. The successful treatment of some cases of cystic fibrosis, as described above, or the soon-to-be-accomplished victory over hepatitis C virus, demonstrates what can be done. But failures in such areas as Alzheimer's disease, heart disease, or the development of an HIV vaccine illustrate both the scientific and business challenges of drug discovery.

[2] This section, including subsections, is based on the presentation by R. Sanders (Sandy) Williams, President, the Gladstone Institutes.

In a 2010 interview, NIH Director Francis Collins described the pressing need for "new paradigms of public–private partnership[s] . . . effectively 'de-risking' projects for downstream commercial investment" (Collins, 2010). New forms of partnerships among academic experts, industry professionals, and public and private sources of investment can improve what Williams and other workshop participants called the "drug development ecosystem." This ecosystem is diverse, encompassing universities, independent research institutions, biotechnology and pharmaceutical companies, voluntary health organizations, foundations, philanthropists, investors, and government. CAN, within the NCATS umbrella and through relationships with other federal agencies and other players in the ecosystem, has an unprecedented opportunity to replace failing processes with effective complementary teamwork, providing measurable results to Congress, to disease advocacy groups, and to the taxpayers who support the effort, said Williams. Academia and industry have differing skills, mindsets, and incentive structures. CAN can help find new and creative ways to form flexible alliances that combine their complementary attributes with funding sufficient to achieve measurable goals. "If we can do that, we can preserve and advance America's leadership position in medical sciences and industry and, most importantly, bring new solutions to the most vexing and resistant medical needs."

To illustrate his points, Williams focused on Alzheimer's disease. More than 5 million Americans are currently living with Alzheimer's disease, and by 2050 that number will climb as high as 16 million. Alzheimer's disease will cost the United States $200 billion in 2012 and $1 trillion in 2050 if nothing changes. Alzheimer's disease plays out within the daunting biological milieu of 100 billion neurons and over 100 trillion synapses in the human brain. A great variety of pathological events occur in the brains of Alzheimer's patients at the cellular and molecular levels, including proteinopathies, vascular insufficiency, and inflammatory responses. "It is little wonder that, time and time again, preclinical research geared largely to test reductionist unidimensional models is not predictive of success with patients," said Williams.

Suggestions for CAN

Williams offered three suggestions for how CAN could address the scientific dimension of what is needed to accelerate cures. First, CAN could support and catalyze research to develop and validate a new generation of animal models created to exhibit clinically relevant phenotypes. This likely will require multiple genetic manipulations that are carefully selected to bring the models into more faithful representation of human disease. For example, CAN could issue a request for proposals to fund

development of better mouse models. Williams suggested that some of the mouse models could then be deployed in an iterative manner to inform innovation in adaptive clinical trials.[3] This concept is being creatively tested at present within the cancer research community, Williams said, but the possibilities may be much broader. In particular, the creativity of academic labs could be released more productively for this purpose, particularly if combined with industrial know-how within an intellectual property landscape that allows industry and academia to collaborate.

Second, CAN could support the revolution in stem cell biology, in which techniques have been discovered that can generate induced pluripotent stem cells that subsequently can be induced to form virtually any differentiated cell type. A next generation of cellular reprogramming techniques is now emerging by which mouse or human fibroblast or white blood cells can be converted directly into a variety of cell types to model human diseases in culture. In particular, reprogrammed human neurons can form multicellular networks and recapitulate important features of neurodegenerative diseases. The extent to which reprogrammed human cells from diseased patients and relevant controls can be useful for target validation, primary and secondary drug screening, toxicology, or other purposes remains to be seen, but CAN could stimulate progress toward this end.

Third, CAN could support newly emerging scientific approaches that can reveal more fully how the targets of medications function within systems, pathways, and networks within cells. An example is the new ability to define the set of proteins within human cells that form physical complexes with the proteins elaborated during HIV infection. CAN could stimulate the creation and validation of this and other enabling platform technologies with the potential to reveal molecular signatures of disease progression and drug responses.

Business Challenges

Challenges exist in the business arena as well as in the science of drug discovery, noted Williams. The vast reservoir of talent, imagination, and expertise in academia could be connected more effectively with the complementary pools of talent, professionalism, discipline, technical prowess, and financial power in companies. As Williams and Susan Desmond-Hellmann wrote in *Science* last year, "needed now are creative programs that transcend the traditional technology transfer functions of non-profit research enterprises to promote fruitful academic/industry partnerships for drug development" (Williams and Desmond-Hellmann,

[3] See later in this chapter for further discussion of the need for and utility of animal models.

2011). Accelerating cures requires deeply embedded partnerships, focused on defined projects and carried out by teams that work together over time.

A number of new and creative relationships of this nature have sprung up around the country, with research responsibilities divided according to each party's individual strengths and capabilities. For example, even in a period of limited funding, CAN could curate, to the extent possible, features of promising and successful alliances among academic, philanthropic, and industry groups and make the compilation of these attributes available as guidelines or templates for best practices that can inform subsequent contractual negotiations.

As CAN's funding increases, the program is ideally placed to develop a diversified portfolio of projects over time. Other worthwhile actions for CAN include

- facilitation of early engagement of industry experts into academic projects,
- rescuing and repurposing of drugs,
- strengthening computational pharmacology, and
- supporting regulatory science.

Williams said that he favors an emphasis on smaller and midsize projects built on investigator ideas as opposed to a few really big infrastructure projects or a few large clinical trials, "but all would be worthwhile."

NUT MIDLINE CARCINOMA AND OPEN INNOVATION[4]

Understanding of the cancer genome has undergone a revolution, said James Bradner, Instructor in Medicine, Dana-Farber Cancer Institute, and Assistant Professor, Harvard Medical School. Hundreds of thousands of somatic mutations in different cancers are known, and hundreds have been identified as the drivers of cancer pathogenesis. But the ability to act on this understanding is in its infancy, Bradner added. A small-molecule therapeutic is available for only about 14 cancer genomic rearrangements or mutations.

Bradner described a very rare and very lethal cancer called NUT midline carcinoma, which affects approximately 100 people per year in the United States. A molecular pathologist at Brigham and Women's Hospital named Christopher French cultivated cells from patients who have the disease, and Bradner and his colleagues used these cells to test

[4] This section, including subsection, is based on the presentation by James Bradner, Instructor in Medicine, Dana-Farber Cancer Institute, and Assistant Professor, Harvard Medical School.

small molecules that would inhibit the cancer. In particular, they focused on a molecule named JQ1, which interferes with a protein called BRD4. Although there was no mouse model to study the cancer, Bradner at the time was caring for a 29-year-old firefighter succumbing to the disease, who provided a cell sample that was successfully grown in laboratory mice. When mice with tumors received the drug, they survived, whereas those that did not receive the drug died.

JQ1 was a prototype drug not yet optimized for drug-like properties such as solubility or oral bioavailability. In order to access the infrastructure required to bring a molecule into the clinic, Bradner and his colleagues decided to be creative. Using Google, they created a registry for people with midline carcinoma, which revealed a lot of information about the disease profile, such as where it is diagnosed and by whom. Many people have the disease but do not know it, Bradner said. "They should, not just because targeted therapy may soon be available, but because this is the poorest prognostic group of all squamous carcinomas, with a 6.7-month median survival."

At a cost of $45,000 to his laboratory, Bradner and his colleagues made the drug freely available to anyone who wanted to learn about its effects in other diseases. A TED lecture on the drug had more than a half million viewers, and at least 200 people wrote to ask Bradner and his team to share the molecule. "They're under no special obligation to call us back, but they almost always do, to share the exciting findings of their research."

In multiple myeloma, JQ1 downregulates what Bradner called "the central horseman of the cancer apocalypse," a gene called *MYC* that triggers growth. Mice with multiple myeloma driven by *MYC* had a complete response. In mixed-lineage leukemia, leukemia cells exposed to JQ1 "forget they're leukemia and become more mature-appearing, normal monocytes," Bradner said. And in Burkitt's lymphoma, the downregulation of *MYC* again demonstrated the efficacy of JQ1. Why particular cancers respond is a major area of ongoing research.

Open Innovation Leading to Bringing the Compound to Humans

Bradner and his colleagues have found through sharing the compound with scientists at other institutions that in 10 to 15 percent of cases of every major form of cancer, the cancer "just melts away to this drug." These data establish a compelling rationale to bring this compound forward into humans, said Bradner. With internal funding from the accelerator program at Dana-Farber, Bradner and chemist Jun Qi led a medicinal chemistry effort that resulted in the creation of 400 to 500 chemical derivates. Ultimately, they were able to produce a stable of drugs of high potency and high stability in pharmacological studies.

Bradner and his colleagues also have taken a creative approach to translation. For example, they determined that Xanax, a bromodomain inhibitor, is very similar to the JQ1 molecule; however, the amount of Xanax that would be needed to be administered to have an effect on cancer would be excessive. A literature search revealed that GlaxoSmithKline had a bromodomain inhibitor for the management of acute septic shock. They negotiated with the company for investigational use in cancer. Although the molecule is 10 times less potent than JQ1 and performs less adequately in the animal models of the disease, it is available for testing in humans immediately.

Bradner cited the development of JQ1 as an example of open innovation, which has been extremely successful in the information technology field. "We are so much smarter than each of us," he said. The drug they were examining was a prototype and immature, but the index technology sparked rapid innovation when it was publicly and broadly disseminated. Bradner termed patent documents and Investigational New Drug (IND) applications some of the best kept secrets in the pharmaceutical world and argued that such documents should be publicly available to all. If findings about other small molecules were publicly available for scientific research, more drugs like JQ1 could be brought to patients much more quickly.

SICKLE CELL ANEMIA AND THE NEED FOR HEDGEHOGS[5]

Sickle cell disease was the first disease discovered to be caused by a genetic mutation—by Linus Pauling in 1949. Yet only one drug had been labeled for use in sickle cell—the anticancer agent hydroxyurea, which does not work for all patients and can have adverse side effects.

Stephen Seiler, Founder, AesRx, described the biotechnology company's efforts to develop a therapeutic specifically for sickle cell disease. The company has put together a multistage, multi-institute, public–private translational research program centered on the compound Aes-103. The members of the collaboration include AesRx, the National Heart, Lung, and Blood Institute, the Therapeutics for Rare and Neglected Diseases program—which used to be part of the National Human Genome Research Institute and is now part of NCATS—the NIH Clinical Center, and the NIH Clinical Pharmacy. Two weeks before the workshop, the collaboration announced that it is starting a clinical trial with sickle cell patients.

The collaboration has made rapid progress. The IND application was filed less than a year after the collaboration was announced, the healthy vol-

[5] This section, including subsection, is based on the presentation by Stephen Seiler, Founder, AesRx.

unteer safety trial was completed in less than 15 months, and the first dose was administered to sickle cell patients in less than 18 months. A successful type C meeting with FDA clarified the clinical endpoints and regulatory pathway, which, Seiler noted, is very helpful in de-risking a drug.

Small biotechnology companies like AesRx have been an important part of the drug development supply chain since the 1970s. They have taken early-stage ideas, typically from academia, and converted them to more mature products. They have then handed these products off to big pharmaceutical companies, have been bought by those companies, or have become fully integrated pharmaceutical companies themselves.

Over the past 5 or so years, this system has undergone a dramatic change, according to Seiler. "The ecosystem has changed so dramatically that it's become doubtful whether companies like us can continue to provide the role that we have traditionally had in the drug development supply chain." Venture capital funds are dramatically reducing their commitment to early-stage biotechnology companies for several reasons, Seiler said. First, the suppliers of venture capital increasingly have required more mature programs, which has put early-stage biotechnology projects beyond venture capital's investment horizons. Also, whether or not the perceptions are correct, suppliers of venture capital perceive there to be more regulatory risk. Finally, venture capital focuses on chasing the "next big thing" and yielding a quick return.

Lessons Learned

Seiler drew several lessons from his experiences developing Aes-103. The first is that a key element for success is to have programmatic and not episodic planning. AesRx started with early preclinical development and had a goal of taking the drug all the way across the biotechnology valley of death, with planning and budgeting done up front for the entire program. This programmatic planning allowed for early investments in resources that will be needed after project initiation but prior to the data emerging from the first experiments.

Another key to success was an effective management team with a genuinely collaborative focus. Good science is a necessary, but not sufficient, condition for success, Seiler said. "Many venture capitalists spend as much time doing due diligence on the management team they're going to invest in as they spend doing due diligence on the science. So if you're trying to set up a partnership, do the due diligence on your partners well."

Flexibility provided the capability to pursue new programmatic insights and unfolding data. The project was run as a virtual model with very low overhead. At the same time, the personnel involved with the

project brought experience with clinical trials from the perspective of many different kinds of companies.

The ingredients that drove the program so quickly and so far were focus and quick and transparent decision making, according to Seiler. He observed that small biotech companies bring incredible focus to a project. He noted that key decisions could be made in less than 2 weeks, adding that management is very impatient to move them forward. In contrast, collaborators at government agencies or in academia have many other responsibilities. Seiler recalled the statement attributed to the ancient Greek poet Archilachus, which is that the fox knows many things and the hedgehog knows one big thing. Programs like the development of Aes-103 "need a lead hedgehog," he said.

One of the corresponding challenges to success was the government procurement process. Because it was a virtual program, some of the pieces had to be procured from contractors, and the procurement process is complicated, expensive, and slow. Another challenge is that diffuse responsibility can make tight budget control difficult.

LEUKEMIA AND LYMPHOMA AND THE NEED FOR PARTNERSHIPS[6]

The goal of the Leukemia & Lymphoma Society (LLS) is supporting advancement of therapies for patients. The resources of LLS to find cures for the hematological malignancies are limited, said Louis DeGennaro, Executive Vice President and Chief Mission Officer, LLS. The society therefore needs to select and prioritize its projects carefully and foster public–private partnerships to drive the translation of science into treatments. One way that the organization selects and prioritizes projects is through a careful examination of the survival rate, age of onset, and incidence of the diseases that fall within its purview. By comparing these factors to the dollars dedicated to those diseases in the current research portfolio, funding can be compared to unmet medical needs. DeGennaro noted that although the analysis is not perfect, it is an example of multiple tools that could be brought to bear to think about how to prioritize where dollars should go in terms of research.

LLS also has a new Therapy Acceleration Program (TAP), which seeks to fill the gap between academic research and new therapies. The program has a dedicated staff that searches for small biotechnology companies with promising assets that have potential. Staff members also mine the society's research grant portfolio for projects that have moved out of

[6] This section, including subsection, is based on the presentation by Louis DeGennaro, Executive Vice President and Chief Mission Officer, the Leukemia & Lymphoma Society (LLS).

basic research and into the development stage. The TAP staff prioritizes the projects and does due diligence of the medicine, the science, and the business in the case of biotechnology companies. In part through accessing outside resources such as medical experts, business experts, and intellectual property experts, the program's funding is distributed not through grants but through contracts with timelines, milestones, deliverables, and cost-sharing components. These contractual standards serve as built-in metrics for every project, to determine how well the project is going. "We bring industry-quality project management to every program," said DeGennaro.

Partnerships

DeGennaro emphasized that cost and risk sharing can work. LLS does not have sufficient resources to fund the full development program, so its goal is to partner with biotechnology and pharmaceutical companies to get the projects through key hurdles. At that point, the companies can approach the capital market to raise additional dollars or partner with another company to continue the project. DeGennaro added that the LLS portfolio of about 14 projects has an annual investment of $16 million, not far from what is currently allocated for CAN.

At this point LLS has more than a dozen drugs in the pipeline. Roughly half are being developed through partnerships with small biotechnology companies. By supporting late preclinical Phase 1 and Phase 2 trials, and even one Phase 3 registration trial, the society has been able to accelerate the rate at which these programs have moved through development. As just one example of success, DeGennaro cited a partnership with Celator Therapeutics to conduct a controlled Phase 2 trial on acute myeloid leukemia. The agent for secondary acute myeloid leukemia resulting from this trial has doubled the number of patients achieving complete remission, cut treatment-related mortality by a factor of five, and tripled the number of patients still alive at a year.

DeGennaro concluded by briefly mentioning a novel partnership among the society, NCATS, and the University of Kansas to repurpose existing drugs to treat hematological malignancies. A memorandum of understanding set objectives and responsibilities, with commercialization a prominent objective. To enable that, the partnership includes a cooperative R&D agreement with NIH to make certain that the intellectual property generated could be used in commercialization. Within 12 months, two Phase 1 clinical trials of existing FDA-approved agents that are being repurposed to treat hematological malignancies have begun.

CROSS-CUTTING ISSUES

During the discussion period, several topics arose that cut across the five talks on approaches to accelerating translational science.

The Alignment of Partnerships and Culture

One sticking point in partnerships is that academic and commercial organizations have very different operating procedures, goals, and metrics of success. University researchers have incentives for the advancement of their students and their own research. Similarly, as Seiler observed, the style of programmatic organization in the private sector is very different from the typical NIH grant cycle.

Williams added that industry has a legitimate but sometimes overstated need for confidentiality. This issue often arises when trying to settle on contract language, where new types of agreements may be needed to get more expertise involved in collaborations. He also noted that science in academia tends to develop through deeply embedded relationships, not through the "short touches" that characterize academic researchers' involvement with industry, such as consulting arrangements or scientific advisory boards.

Bill Chin, Harvard Medical School, noted that many of the obstacles to collaboration reside in academia and not in industry, saying that behaviors reinforced over time in academia can be obstructive to getting groups together. For example, most university researchers have little understanding of what biotechnology companies actually do and of the levels of expertise, creativity, and imagination that are required. "There's a tendency to think of the latter stages of the development pathways as turning the crank on routine, uninteresting work, and that's a misperception." He also said that academic researchers have a tendency to overvalue what they have, "and therefore they don't come to the table with realistic views."

DeGennaro emphasized the importance of better training for clinical investigators about the regulatory process. "The more of those clinical investigators we can train, and the better they understand the regulatory process and their obligations, the faster the trials can get conducted." A particularly promising approach is to make use of the CTSAs to align the training and the education of a large number of clinical investigators toward regulatory science.

The Use of Animals

Boger remarked that Vertex has put three drugs into the market and none has had an animal model. He termed animal models "overrated,"

because they do not take into account the complexities of the system that dictates drug responses in humans.

Bradner pointed out that the successful development of cancer drugs has for years relied on the early assessment and demonstration of a therapeutic window in animal models. Animals obviously are used as sparingly as possible, but for drugs relying on new mechanisms, establishing the therapeutic value in animals has been valuable. On the other hand, he noted, there is no obvious animal model for sickle cell disease, but that has not been a barrier to moving the science forward.

Williams sought to distinguish the demands of the science from the demands of regulation. He said that although animal models are not required for drug development, each situation has different requirements. Some diseases will have more authentic animal models that produce evidence capable of overcoming the obstacles to a cure. He argued for an integration of all of the tools that could be applied.

Cool Tools

The presenters also discussed the "cool tools" that Kathy Hudson, NIH, called for in her opening remarks. Bradner said that tools could be "absolutely revolutionary" if they could perform the exhaustive and expensive predictive toxicology studies mandated in regulatory pathways at an early enough stage to prompt candidate selection. "Any of these technologies that can be released early on regarding drug metabolism would be hugely beneficial to our work."

As an example of a cool tool, Tom Insel, NCATS, mentioned the NCATS pharmaceutical collection, which is a collection of all approved compounds in Europe, the United States, and Asia. Currently almost 4,000 compounds are in a repository and can be used to go directly from an approved compound to a new indication. He also mentioned the hundreds of thousands of compounds in a molecular libraries program that are publicly available as part of the National Chemical Genomics Center at NCATS, which NCATS will continue to streamline.

Among the other tools, methodologies, and approaches mentioned by presenters were

- systems pharmacology,
- models representing various biological processes,
- informatics,
- crowdsourcing,
- prizes,
- small-molecule databases,
- chemical probes, and
- collaborative tools.

3

Application of Matching Authority

Key Messages[a]

- Matching requirements provide funding agencies with opportunities to leverage their resources and receive input from third-party investors.
- Matching requirements can create incentives to engage companies early in the development process and help to ensure their commitment to follow-on financing in later stages of development.
- Agreed-upon milestones can provide structure to partnerships and maintain the focus on progress.
- Funding agencies could use a matching authority to proactively encourage collaboration between academics and industry.

[a] Identified by individual speakers.

The section of the CAN authorizing legislation establishing the Cures Acceleration Partnership Awards states: "An eligible entity shall contribute to the project non-Federal funds in the amount of $1 for every $3 awarded . . . except that the Director of the Center may waive or modify such matching requirement in any case where the Director determines that the goals and objectives of [the awards] cannot adequately be carried out unless such requirement is waived" (see Appendix B).

This matching authority was the subject of a session at the work-

shop. Three speakers explored existing efforts across other federal and state agencies in which a matching authority or a similar requirement is applied. The session also featured speakers representing different organizations that could be called upon to provide a match, including venture capital and the pharmaceutical industry. Together, the speakers examined the benefits and advances that have been achieved through current applications of matching authority and the steps that have been taken to overcome barriers. As the moderator of the session, Nancy Sung, Burroughs Wellcome Fund, said, "We want to milk as much as we can from those examples so that we can incorporate their lessons learned into the early planning stages for CAN."

THE SMALL BUSINESS INNOVATION RESEARCH PROGRAM AT THE NATIONAL CANCER INSTITUTE[1]

The National Cancer Institute (NCI) Small Business Innovation Research (SBIR) program is not set up exactly like the matching authority given to CAN, but it offers lessons that apply, said Michael Weingarten, Director, SBIR Development Center, NCI. The SBIR program is a congressionally mandated set-aside program for small business concerns to engage in federal R&D with the potential for commercialization. In FY 2012, 2.6 percent of the overall NIH budget is required to be set aside for the program. The similar Small Business Technology Transfer (STTR) program, which is designed to facilitate cooperative R&D between small business concerns and U.S. research institutions, has a set-aside of 0.35 percent of the overall NIH budget. Together, these programs represent $115 million at NCI.

The programs are divided into three phases. In the SBIR program, Phase I is a feasibility study, typically 9 to 12 months long, with an average budget at NCI of about $150,000. If successful, this is followed by a Phase II SBIR, which requires a commercialization plan and is typically about $1 million over 2 years, though projects at NCI can be as much as $2 million in total award size.

Phase III is the commercialization stage. It is expected to be done by companies using funds separate from the SBIR programs, whether from venture capital, another company, or some other strategic partner.

The Importance to NCI

The SBIR and STTR programs are the primary resource at NCI for enabling the commercialization of high-impact technologies that can ben-

[1] This section, including subsection, is based on the presentation by Michael Weingarten, Director, SBIR Development Center, National Cancer Institute (NCI).

efit patients, said Weingarten. Examples of these technologies involve small molecules and biologics, cancer diagnostics, cancer imaging, and electronic health and education tools. Projects undergo NIH's rigorous scientific peer review.

These programs are also important to small business, especially with the decline in venture capital in the life sciences since 2008. They are a stable and predictable source of funding and currently are one of the largest sources of early-stage life sciences funding in the United States. Intellectual property rights are retained by the small business concern. It is not a loan; therefore, no repayment is required. NCI does not take any kind of equity position in the business, so the federal funding is nondilutive capital and can be a leveraging tool to attract other funding.

Weingarten concentrated specifically on the part of the SBIR program at NCI known as a Phase II Bridge Award, which addresses the gap, or valley of death, between Phase II and commercialization. The Bridge Awards are intended to help companies that were getting promising results from SBIR funds in Phase II but find that they are running out of capital before they are able to commercialize those results. Companies can apply for up to $3 million in additional NCI funding over a 3-year period, with an additional peer-review cycle to evaluate progress and future plans. The objective is to accelerate commercialization by encouraging third-party investors and strategic partners to form partnerships earlier in the development process. NCI deploys a "match-like" mechanism in that it gives competitive preference and funding priority to applicants that can raise substantial third-party funds (i.e., greater than the amount received from NCI).

The preferred types of third-party funds include cash, liquid assets, or convertible debt. Third-party investors can be other companies, venture capital firms, angel investors, universities, state or local government, or any combination of these and other investors.

The program was initiated 3 years ago, and 12 projects have been funded to date. Three are in the area of therapeutics, six involve imaging technologies, and three involve molecular diagnostics.

NCI is investing a total of $31 million in these projects across its portfolio. The companies, in turn, have raised more than $72 million in funds from third-party investors. Approximately one-third of this funding is from venture capital, one-third from strategic partners, and one-third from individuals, primarily angel investors. "That means that the NCI is getting more than a two-to-one leverage out of the funds that we are putting into each of these different projects," Weingarten noted.

The benefit of this competitive funding preference is that it provides NCI with an opportunity to leverage millions of dollars in external resources. It also produces valuable input from third-party investors. If

venture capitalists or companies are evaluating whether to invest jointly in a project, they will submit a company to rigorous commercialization due diligence prior to the award. They also are likely to be heavily involved in providing commercialization guidance over the course of the award. And they are likely to be involved for longer than the Bridge Award project period.

The third-party investor benefits through the opportunity to partner with small businesses to develop and commercialize projects that have been vetted by NIH peer review and for which substantial proof-of-concept data already exist.

The portfolio for the program is structured so as to focus on projects that require FDA approval. Of the 350 to 400 ongoing projects at any time, the Bridge Awards program has the potential to influence about three-quarters of the Phase II projects in NCI's SBIR portfolio, said Weingarten.

Weingarten pointed to the special review potential Bridge Award projects undergo as a key to the program's success. Review panels include venture capitalists, clinicians, pharmaceutical industry professionals, and academics. The review also emphasizes important commercialization considerations such as intellectual property positions and strategies for gaining FDA approval.

THE MATCHING REQUIREMENT AT THE CANCER PREVENTION AND RESEARCH INSTITUTE OF TEXAS[2]

The Cancer Prevention and Research Institute of Texas (CPRIT) was created by a statewide vote in 2007. Funded by general obligation bonds, CPRIT is investing $3 billion in cancer prevention and research through 2021. At the time of the workshop, it had funded 387 awards totaling $670 million.

The goals of CPRIT are to expedite innovation and commercialization in cancer research, enhance access to evidence-based prevention programs and services throughout the state, and attract top talent and create high-quality new jobs in the state. Funds have gone to community organizations, academic institutions, and companies. About 20 percent of funding has gone to companies or private-sector incubators, with a particular emphasis on helping companies traverse the valley of death. The remainder of the funding goes to academic institutions. For example, one of the biggest awards to date has been to the Statewide Clinical Trial Network of Texas, which is seeking to establish a clinical trial network across Texas run through local communities rather than just through big cities.

[2] This section is based on the presentation by Kristen Doyle, General Counsel, Cancer Prevention and Research Institute of Texas (CPRIT).

Kristen Doyle, General Counsel, CPRIT, stated that the matching requirement written into the legislation provides the following: "Before the Cancer Prevention and Research Institute of Texas may make a grant of any proceeds of the bonds issued under this section, the recipient of the grant must have an amount of funds equal to one-half of the amount of the grant dedicated to the research that is the subject of the grant request."

The provision applies only to the cancer research and commercialization grants, not any prevention grants awarded by CPRIT.[3] The matching funds can come from any source, not just the institution or company receiving the award. In some cases, awards have been delayed while awardees arrange for the match, but in no case has a company or university not been able to receive funds from CPRIT because they did not have a match, Doyle said. Matches also can be made on an institutional or organizational level rather than project by project, because some institutions receive multiple awards from CPRIT.

As part of applying for a CPRIT grant, proposals receive a scientific review, a commercialization review, and an intellectual property review. These reviews can help awardees find matching grants in subsequent applications, said Doyle. CPRIT also has an acceleration program that can facilitate relationships to acquire matches. Doyle characterized her program as intended to be a "one-stop shop" for companies interested in working with universities.

Matches are certified through the contracting process. They can be certified for the total award amount or on a year-by-year basis. The annual reporting process requires an audit if an institution receives more than $500,000 from CPRIT.

Some of the flexibility built into other matching programs is not present in CPRIT, Doyle said. The match cannot be waived by the director, and the match has to be of funds and not in-kind costs (though she noted that this provision will be reviewed in the future).

All CPRIT contracts are public, as are deliverables, timelines, and metrics of progress. Strategic plans and progress reports are made to the state legislature.

THE MATCHING REQUIREMENT AT THE CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE[4]

The California Institute for Regenerative Medicine (CIRM) is a taxpayer-supported research institute approved by California voters in

[3] The legislation provides that up to 10 percent of the award can go to cancer prevention.

[4] This section, including subsections, is based on the presentation by Ellen Feigal, Senior Vice President, R&D, California Institute for Regenerative Medicine (CIRM).

2004. It is funded through $3 billion of state obligation bonds for research in California at a maximum level of $300 million per year. The overall goal of CIRM is to create an environment that supports both public- and private-sector research into life-saving and life-improving therapies for patients based on stem cell science. "This was really to provide a safe haven to work on this innovative technology," said Ellen Feigal, Senior Vice President, R&D, CIRM.

CIRM is designed to build research excellence and encourage the translation of discoveries to clinical opportunity. Prominent emphases for CIRM have been partnerships and facilitating pathways into the clinic. It has received great support from the public, industry, universities, and patients, according to Feigal, who also noted that it is an unusually transparent institution, with review decisions, project summaries, and many other sources of information posted on its website.

At the time of the workshop, CIRM had awarded more than 450 research and facilities awards to 59 different institutes and companies. It had contributed to 12 new state-of-the-art research centers of regenerative medicine and had supported 62 translational programs across a spectrum of disease areas. Fourteen disease teams had received awards of up to $20 million aimed at first-in-human trials within 4 years. A new set of disease teams and strategic partnerships are being funded in 2012. Projects extend from basic research to Phase 2 clinical research, and CIRM has partnered with other agencies and organizations worldwide. CIRM has so far allocated $1.3 billion of its $3 billion total budget.

Matching Requirements at CIRM

Feigal discussed CIRM's use of a matching authority in four areas: facilities; translational and developmental research programs; collaborative funding programs; and leveraging initiatives with public and private institutions, foundations, industry, and other government agencies.

CIRM has devoted approximately $270 million to 12 state-of-the-art facilities, and institutional and private donors have put in the remainder of up to $1 billion. These funds have covered one-time space development and renovation costs for capital project proposals in each of three categories—basic and discovery, preclinical, and preclinical development and clinical. CIRM required matching funds in cash of at least 20 percent of the grant amount for facilities. Funding from other sources above the cash match was considered project leverage, and this was part of the basis for the competitive evaluation.

CIRM is funding 14 multidisciplinary translational and developmental research disease teams. Matching is not required, but matching has been provided by one company, and five other disease teams have lever-

aged money through their collaborative funding partners for partnered research in other countries. These awards all have mutually agreed-upon milestones that must be met before CIRM dollars are released, with evaluation by CIRM staff and external experts.

The CIRM oversight board is determining a new set of disease teams in 2012, which will do preclinical development or conduct and complete clinical trials. While raising matching funds is not required, it is a review criterion, so that proposals that incorporate a match will be more competitive than those without matching. Matching funds are expected to come from the biotechnology and pharmaceutical industries and should be at least one-to-one. CIRM is recommending that nonprofits partner with industry or other investors to obtain matching funds.

CIRM's newest initiative is a targeted clinical development program aimed at completion of clinical trials. It requires at least a one-to-one match up to $25 million over 3 years. As with the other programs, mutually agreed-upon milestones and evaluation processes are built into the program. In addition, CIRM is supporting a strategic partnership fund that covers the valley of death—or, as Feigal recast it, the "bridge to cures." The goal of this program is to attract industry engagement and investment in CIRM-funded research so that industry is involved early and provides regulatory, scientific, technical, and business expertise. The program requires evidence of commercial validation, based either on the financial strength of the applicant or on co-funding from an industrial or venture capital partner. It also has a one-to-one match requirement, up to $10 million over 4 years, with all of the industry dollars going to direct costs.

To date, CIRM has $138 million in total commitments in response to its request for applications by collaborative funding partners. Twenty collaborative research teams have successfully competed, and $60 million has been provided by collaborative funding partners. About $200 million in collaborative funding partner and CIRM awards has been made to date.

Advantages and Opportunities of Matching

Feigal listed several considerations that went into the application of matching requirement. Matching has the advantage of leveraging CIRM's investments and sharing risk. It enables critical early development programs for therapies, especially with financial disbursements linked to progress on mutually agreed-upon milestones. It engages industry early in the development process, which helps to ensure industry commitment to follow-on financing of later-stage clinical development if milestones are met. "We don't want to do these things just as research experiments," said Feigal. "We want there to be a full development path toward approval." A matching requirement facilitates collaborative work with the best inves-

tigators in the world, with partnerships structured primarily through state or national government funding agencies using memoranda of understanding. CIRM helps prospective grantees find potential matches. Indeed, companies occasionally approach CIRM to inquire about research they could sponsor.

Feigal also listed several lessons learned. Academic researchers and nonprofit organizations may not be able to compete, or at least are challenged, in meeting match requirements for early-stage research. Similarly, small biotechnology companies and start-ups can be challenged in a very difficult economic environment for innovative technologies. In these circumstances, funding agencies need to be proactive in encouraging collaboration between academics and industry. Academics need help with resources and skill sets that can attract industry partners and other forms of investment. And industry needs to be engaged through initiatives that take into account the timeframes conducive to development and commercialization. "What we are trying to do as much as possible is position our teams for success."

Another lesson Feigal emphasized is the value of agreed-upon milestones in maintaining focus. During the conduct of research, CIRM scientists and funded research teams have ongoing discussions, and updates on progress are made on a quarterly, biannual, and annual basis. CIRM also has publicly available 1-year and 5-year goals, with metrics to determine whether those goals are being met.

Finally, Feigal cited the importance of a collegial and professional relationship with FDA. FDA personnel participate in educational webinars and roundtables and see such interactions as a two-way street, such that FDA staff can also learn from CIRM-funded investigators.

PERSPECTIVES OF MATCHERS

Three representatives of organizations that would be called upon to provide matching funds under CAN provided their perspective on matching requirements for biomedical research.

Jens Eckstein, President, SR One, which is the corporate venture arm of GlaxoSmithKline, said that his organization looks for breakthrough innovations in application of the belief that breakthrough innovation will become strategy. He and his colleagues are interested in therapeutics, imaging, diagnostics, technology, software—"anything that will change the way medicine is done." SR One has been one of the most active venture groups in recent years in early-stage investing, and it is one of few companies that will start companies. SR One also has a $1 million fund to support what Eckstein called "killer experiments" even before a company is formed. The company has relatively deep pockets, trying to

spend $30 million to $50 million per year and staying with companies for protracted periods.

Eckstein argued that there are actually two valleys of death. One is the valley of death perceived by entrepreneurs and principal investigators who want to start companies and feel that they cannot get early-stage funding. The problem with early-stage funding, said Eckstein, is that 8 out of 10 academic experiments do not reproduce, either because experiments can succeed only when done by one person, or because proper controls are lacking. If an early-stage idea leads to a killer experiment that reproduces, the probability of getting funding is good.

The second valley of death is perceived by investors who fear that an early-stage idea will not get to "proof of relevance." Eckstein noted that he uses the term "proof of relevance" instead of "proof of principle" because "scientific efficacy is no longer good enough." An innovation "has to be relevant for the patient, for the payer systems, for the whole health care system. Whatever the result is, it needs to fit into the whole equation."

Martin Lehr, Associate, Osage University Partners, said that his fund partners exclusively with U.S. universities. It works closely with technology transfer offices at 44 private and public research institutions to find up-and-coming technologies in the physical and life sciences. The fund believes that universities are very good at creating technologies that lead to start-up companies that make money for investors, and "a select assortment of schools do it at an incredibly high velocity."

Lehr looks for three things when choosing academic technologies in which to invest. Is the technology in an attractive area? Is it sufficiently de-risked? And is it of strategic value? He noted that people associated with universities typically are unable to answer these three questions, because they have not been trained to do so. Academic researchers have been trained to do experiments that are relevant to themselves and to their colleagues, Lehr said. They generally do not have incentives to think outside the box about the wider value of a technology.

Finally, Michael Gutch, Managing Director, MedImmune Ventures, which is the corporate venture arm of the AstraZeneca Group, said that his organization seeks to build relationships not only with the companies in which it invests but with the companies in which it chooses not to invest. "In the course of a year, we may see 500 deals. We may invest in three or four, but we try to build relationships across many of the companies that we do see."

MedImmune Ventures is expanding its investments beyond therapeutics to technologies that affect the discovery, development, or commercialization of therapeutics such as diagnostics, imaging, and information technology. But the reality of the venture capital environment is that investments in health care are shrinking. Private venture capital firms in

particular have had trouble generating financial returns and have been leaving the field to corporate venture capital.

In such an environment, partnerships among groups will be critical for early-stage technologies and companies, said Gutch. In some sense, venture capitalists are risk averse, in that they try to minimize both financial and regulatory risk by syndicating their investments—that is, investing alongside others to put less of their capital at risk. Venture capitalists want to partner with foundations, governments, and other organizations, even though those organizations tend to have different agendas. For example, MedImmune had a relationship with CPRIT through an Austin-based medical device company, "and that was a very productive relationship. So it can work."

The individual panelists offered the following suggestions and opportunities for CAN:

- Eckstein said that CAN could educate the participants in potential partnerships about what information is confidential and what information is not confidential. He said that much more can be treated nonconfidentially than is the case today, which would encourage "great conversations."
- The greatest opportunities today are in new areas of convergence, Eckstein said. These convergences may be between and among technical areas, diagnostics, imaging, biomarkers, drug discovery, and so on. For example, one especially promising convergence is between outcomes, the strategy of clinical trials, and research, where patient data and clinical outcomes can inform early-stage investments.
- Lehr suggested that a valuable role for CAN would be to provide funding for academic researchers to work with people in industry. For example, academic researchers could be supported to interact with people in the pharmaceutical industry to get insights into what is valuable to them, so when new technologies are developed, industry will be ready to fund them.
- According to several panelists, CAN could offer a "one-stop shopping" matchmaking function to help centralize and streamline the partnering of scientists and funders from all sectors and settings. Several panelists also added that CAN could contribute by supporting or facilitating training opportunities to clarify boundaries for appropriate nonconfidential interactions that do not require continual legal analysis and are not hindered by overconservative interpretation.

4

Application of Flexible Research Authority

Key Messages[a]

- The flexibility and freedom from government contracting regulations available through exercising OTA can attract companies to public–private partnerships that would not otherwise accept government contracting restrictions.
- Because agreements negotiated under OTA can take extra time, gathering together all of the parties with interests in the negotiations can speed the process.
- A close and effective relationship between the program manager and contract officer can both shape and ease the process of arriving at an OTA agreement.
- Given the level of expertise that industry brings to the negotiation of an OTA agreement, it is important that OTA negotiators and staff supporting the program have a high level of expertise.

[a] Identified by individual speakers.

The section of the CAN authorizing legislation establishing the Cures Acceleration Flexible Research Awards states: "If the Director of NCATS determines that the goals and objectives of this section cannot adequately be carried out through a contract, grant, or cooperative agreement, the Director of the Center shall have flexible research authority to use other transactions to fund projects in accordance with the terms and conditions

of this section. Awards made under such flexible research authority for a fiscal year shall not exceed 20 percent of the total funds appropriated" (see Appendix B). This provision enables CAN to use contracting procedures known generically as OTA, which has proven to be a useful tool at DARPA and other federal agencies that are authorized to use OTA. A session at the workshop featured speakers from several of these agencies: DARPA, the Advanced Research Projects Agency–Energy (ARPA-E), BARDA, and DTRA. The speakers described the advantages and disadvantages of OTA and the ways in which it could be used at CAN.

OTA AT DARPA[1]

In the 1980s, it became apparent that in some areas civilian technology was rapidly outpacing military technology. Companies producing products for the civilian market were intent on introducing products into markets quickly and inexpensively, whereas it was found that defense contractors worked more slowly and expensively. At the same time, the defense industrial base was shrinking, forcing more reliance on commercial firms. Public–private partnerships were becoming more common, as exemplified by the Sematech collaboration in the semiconductor industry, to which both government and the industry devoted $100 million per year.

Many civilian firms with large R&D budgets were reluctant to do business with DoD, observed Scott Ulrey, Deputy Director, Contracts Management Office, DARPA. Large companies did not want to subject themselves to the terms of FAR, which apply to government purchases of goods and services. FAR was originally designed to enable all government agencies to work under the same provisions, but over time the document grew. Today, the number of regulations is "literally staggering," said Ulrey, requiring considerable expense for companies to comply.

To help facilitate government contracting with civilian companies while minimizing the administrative burden, legislation passed in 1989[2] permitted the secretaries of military departments to "enter into transactions (other than contracts, cooperative agreements, and grants) for basic, applied and advanced research projects." This OTA confers great flexibility upon program managers and contracting officers in setting up an agreement that meets the needs of a given project. "There is no one way to do an other transaction. I keep hearing about new ways of doing things all the time, and I say, 'Go for it.' Whatever makes good business sense, go ahead."

[1] This section, including subsections, is based on the presentation by Scott Ulrey, Deputy Director, Contracts Management Office, DARPA.

[2] 10 U.S.C. § 2371.

The legislation also requires that "to the extent . . . practicable, the funds provided by the government do not exceed the total amount provided by other parties to the other transaction." In effect, this provides for a 50 percent or more cost share, ensuring that the commercial partners have a stake in the project. Ulrey noted that this "resource sharing" can be in the form of cash or in-kind.

Types of Other Transactions

The two most common types of other transactions at DARPA are Technology Investment Agreements (TIAs) and other transactions for prototypes:

- TIAs support the development of technology. They are authorized by Part 37 of the DoD Grant and Agreement Regulations,[3] the current version of which is from August 2007. These are the types of agreements that are most likely to be used by CAN, Ulrey said.
- Other transactions for prototypes are authorized by Section 845 of the National Defense Authorization Act for FY 1994. They are used for developing a prototype technology such as an unmanned aerial system. In this case, the government is buying a good or service for its direct benefit.

DARPA uses two solicitation types with other transactions:

- Research announcements are directed toward grants, cooperative agreements, and TIAs. These solicitations can specify such aspects as cost sharing and team arrangements. They are very different than requests for proposals, according to Ulrey, in that the government specifies a problem and asks for solutions to the problem.
- Program solicitations are typically used for other transactions for prototypes. They typically specify performance or objectives and tend to have a less-defined structure.

Benefits of OTA

The use of OTA has several benefits, according to Ulrey. First, participating companies are not bound by most procurement laws and regulations, though they are bound by other regulations tied to appropriations, such as the Civil Rights Act or lobbying restrictions.

[3] 32 CFR subchapter C (Parts 21–37).

OTA also allows for competition to the maximum extent practicable. Ulrey tries "to push for competition in 99.9 percent of cases. It's very rare that we do a sole-source effort. We want to get as much competition as we possibly can, [though] it's not always possible in the DoD environment."

Flexibility regarding intellectual property is very attractive to companies, said Ulrey. Unlike OTA agreements, grants and contracts need to comply with the Bayh-Dole Act, which can be restrictive on companies, even though they retain title to inventions. Grants and contracts also do not permit the retention of trade secrets, which can be a powerful disincentive for companies to participate in government research. OTA avoids these restrictions, though the government retains certain rights to technologies if companies do not pursue the technologies further.

OTA does not have termination for default or termination for convenience, which are unilateral rights specific to government contracts. Government agencies still have termination rights under OTA, but they are negotiable.

OTA encourages the use of what are called payable milestones. These are developed by the program manager and contracting officer to link payments with measurable events rather than solely with the submission of a status report. They allow flexibility and cost savings by reducing timeframes for technology development and encouraging streamlined ways of operating.

Under OTA, there are no mandatory cost principles or accounting standards, except for generally accepted accounting principles, which is much more acceptable for companies.

OTA allows companies to hire their own independent public accountant rather than having their books examined by the Defense Contract Audit Agency. It also does not require the use of the government system for subcontracting associated with FAR. Management structures are flexible so long as sound business judgment is maintained.

Creating Incentives for Investment

All of these advantages make government funding under OTA more like an investment in the development and commercialization of technologies. Government intrusion and red tape are minimized and cooperation is encouraged. At DARPA, authority for negotiating and approving OTA agreements is pushed down to the lowest level possible so that high-level approvals are not necessary. The flexibility of OTA also makes it possible to enter into relationships with unconventional partners, such as hackers or organizations that offer prizes for particular technological accomplishments. "We want to make it easy," Ulrey said. "We would rather you focus on developing the technology than worry about complying with regula-

tions. . . . If we want commercial companies to do business with us, we have to operate in a more commercial fashion."

"I always start these negotiations with the phrase that we are never going to write a perfect agreement," Ulrey said. "There are 999 ways of tripping each other up on this instrument. They are good-faith instruments. Everyone has understood that from the onset. But we have never had one protest on an other transaction . . . [or] any real problems working with commercial industry."

A disadvantage Ulrey cited is the amount of time that can be spent negotiating under OTA. When everything is negotiable, some points may require extended discussions. Ulrey noted that this can be addressed by getting everyone who is involved into the same room, including program managers, lawyers, and contracting officials, rather than having the parties work in isolation and sending proposals and proposed changes to the others.

Program Managers and Contract Officers

Also from DARPA, Daniel Wattendorf said that he had used OTA during his 2 years at DARPA. The decision of whether to use OTA depends on the project, and projects at DARPA differ greatly in size, scope, and intent. Wattendorf noted that he talks with the contract officer at length very early in the process, close to the point of concept of a program. This approach, which is characteristic of the team-based environment at DARPA, forms a close relationship between the program manager and contract officer that can shape the use of OTA. OTA has been extremely useful, Wattendorf concluded, but, he observed, he would not enter into it without having a contract officer who is very comfortable doing one of these agreements.

The situation is different than at NIH, Wattendorf said. In his opinion, it is easier to work with industry at DARPA than with academia at NIH. Industry understands the demands of R&D as a business process. With academic researchers, aspects of the process such as milestones may be less carefully observed.

ARPA-E AT THE DEPARTMENT OF ENERGY[4]

ARPA-E, at the Department of Energy, was modeled after DARPA and first received appropriations in FY 2009. ARPA-E has used its OTA authority three times, under a TIA arrangement, said Peder Maarbjerg,

[4] This section is based on the presentation by Peder Maarbjerg, Assistant Director for External Coordination, ARPA-E.

Assistant Director for External Coordination, ARPA-E. For all three of the TIAs, the only provisions that were modified were intellectual property provisions, with none of the TIAs providing for a complete waiver of intellectual property rights.

Maarbjerg explained that, with typical contracts, the government retains two kinds of ownership rights. The first is known as government-use license—the U.S. government has a royalty-free license to use a patented technology for government purposes. For example, the government could license a company to manufacture the patented technology for use by the U.S. military, but not for commercial sales.

The second ownership right is known as march-in rights. Under a march-in provision, if the patent owner does not commercialize the patented technology, the government has the right to license the patented technology to a commercial competitor to ensure that the taxpayer-funded technology reaches the marketplace. This provision can dissuade some prospective private-sector partners, Maarbjerg noted. He added, however, that the U.S. government has never exercised its march-in rights. "It makes sense. If you run into an inventor who went through the whole process of applying to the federal government and getting the grant and doing the work, he's not going to put it on the shelf."

In two of the three cases where ARPA-E used a TIA, companies were concerned that the government's march-in rights would inhibit their efforts to raise private capital or to develop additional uses for the technologies. To address this concern, ARPA-E agreed to include a provision that would give the company the option to buy back the government-use license and march-in rights. Under this option, the company would have to repay all the ARPA-E funds received under the award plus interest and further agree to forgo any ARPA-E funding under the award in order to buy back the government-use license and march-in rights.

In the third case, a company was concerned that some of its intellectual property that had been developed before the ARPA-E award would be seen as part of the whole, thus subjecting the older intellectual property to the government-purpose license and march-in rights. To address this concern, ARPA-E used a TIA to agree that the government-purpose and march-in rights would apply not to prior intellectual property but only to inventions conceived during the award.

Like DARPA, ARPA-E typically announces a goal that it wants met and solicits short concept papers about how to meet that goal. If these concept papers are encouraging, a full proposal is requested. This proposal is then submitted to review by industry, government, and academia, and reviews are sent to the author of the proposal for rebuttal.

OTA is a tool and not an end in itself, Maarbjerg emphasized. Universities often are more comfortable working with FAR and not starting

from a blank piece of paper. But ARPA-E often engages very large firms that would not normally work with the federal government. If a firm is nervous about partnering with government, OTA may be a way to allay its concerns.

PROMOTING AN EFFECTIVE MEDICAL COUNTERMEASURES ENTERPRISE AT BARDA[5]

BARDA of the U.S. Department of Health and Human Services has OTA but has never used it, said Gerald Kovacs, Director of the Division of Chemical, Biological, Radiological, and Nuclear (CBRN) Countermeasures, BARDA. The scope of BARDA's mission includes bridging the entire valley of death from preclinical studies to Phase 3 studies, licensure, and procurement. "Unlike you all, I hope that we never have to use the products that we're developing and stockpiling," said Kovacs, but BARDA's experiences also offer important lessons for commercial drug development.

BARDA's mission is "to develop and provide countermeasures for CBRN threats, pandemic influenza, and emerging infectious diseases by product development, stockpile acquisition/building, manufacturing infrastructure building, and product innovation." Its current budget is $1.6 billion, with an additional $5.6 billion in a special reserve fund for Project BioShield, which is designated for licensure, production, and delivery of medical countermeasures. If a project fails, said Kovacs, it should only be the result of failure of the product to achieve the desired safety or efficacy thresholds, and not as a function of an inability to provide the proper support from a technical, business, and regulatory perspective.

The Department of Homeland Security has identified 13 material threats to the health and economy of this country. Those 13 threats all require either a vaccine or a therapeutic, and most require a diagnostic. Given the price of moving a drug from Phase 1 to licensure, "the $1.6 billion is probably not even one-tenth of the amount that we would need to fund this pipeline," said Kovacs.

BARDA's strategic plan calls for it to achieve "an advanced development pipeline replete with medical countermeasures . . . emphasizing innovation, flexibility, multipurpose, broad spectrum application, and long-term sustainability." An important authority granted by the legislation governing BARDA is emergency use authorization (EUA). In creating

[5] This section, including subsections, is based on the presentation by Gerald Kovacs, Director of the Division of Chemical, Biological, Radiological, and Nuclear (CBRN) Countermeasures, BARDA.

EUA, Congress permitted FDA to allow unapproved medical products or unapproved uses of approved medical products to be used in an emergency to diagnose, treat, or prevent serious or life-threatening diseases or conditions caused by such agents, when there are no adequate, approved, and available alternatives. In addition, legislation has limited the liability from countermeasures developed by BARDA.

BARDA has defined the importance of threats and has developed a portfolio of products to deal with those threats. It also has been developing a pipeline of medical countermeasures that are early in their development cycle. Most products cannot be tested in humans for safety and efficacy, so a parallel track of research has been developing animal models to use as surrogates for human clinical testing.

Public–Private Partnerships

Notably, Kovacs commented that although technically BARDA has OTA under the Pandemic and All-Hazards Preparedness Act of 2006, OTA has never been deployed by the program. Instead, Kovacs offered models and lessons learned from the BARDA experience using FAR to foster innovation and development.

The 2009 influenza pandemic brought new initiatives not just to BARDA, but to FDA, NIH, and CDC. Partnerships with private industry were emphasized, as were broad-spectrum drugs to reduce costs and expand preparedness. BARDA also began giving more thought to how to respond either to a pandemic or to an emerging infectious threat. For example, because of the risk to the pharmaceutical industry of developing antibiotics, BARDA has partnered with industry to develop antibiotics not just for epidemics but for biothreat agents. The agency also has taken an approach to product development whereby projects are killed as early as possible to reduce expenditures of money and effort on projects that are not performing properly.

BARDA relies on a variety of mechanisms to fulfill its mission, including contract research, contract manufacturing, and technology transfer. This range of activities can be daunting for small biotechnology companies, which typically want to take a drug all the way from the research laboratory to use. It also makes rapid-go/no-go decisions through what is called in-process review, where interagency partners meet to determine whether a performer has met the milestones in a contract and whether the work should go forward.

BARDA's core services include regulatory and clinical affairs, an animal studies network, a manufacturing network, centers for innovation in advanced development and manufacturing, and technical expertise. BARDA staff includes people who have worked in industry and thus have

seen products developed and have licensed products themselves. BARDA also has established public–private partnerships for pandemic and seasonal flu vaccines manufacturing and for anthrax vaccine manufacturing, both using cost-sharing mechanisms.

Lessons Learned

Kovacs concluded with 10 lessons that he has learned during his time with BARDA:

- Agency staff needs to include experienced professionals who understand drug development.
- Bureaucracy needs to be minimized, with an emphasis on progress over process.
- An infrastructure of accountability needs to be established for decision making.
- Instead of reinventing ideas, connect with other agencies working with the same or similar mission, especially FDA.
- Implement project management that is up to industry standards, with project coordination teams and clearly defined metrics.
- Contracting staff are integral to success and can exercise enormous creativity.
- Proposals should be developed in close collaboration with program managers and with transparency.
- Solicitations can be creatively applied. BARDA has used the mechanism of the "broad agency announcement," which solicits and quickly reviews white papers; submitters of those white papers found to have promise are invited to submit a full proposal.
- An "open door" mechanism can bring in ideas and projects.
- Establish firm relationships with congressional representatives and their staffs.

OTA AT DTRA[6]

Jason Paragas, Special Assistant to the Director, DTRA, described the lessons his agency has learned from its experiences with OTA.

First, as noted by other speakers in the session, the process of approving OTA agreements is slow. Using OTA opens many issues to negotiation, and coming to agreement on each of these issues takes time.

However, this process also provides advantages, Paragas noted. First,

[6] This section is based on the presentation by Jason Paragas, Special Assistant to the Director, DTRA.

it can involve people from industry who are skilled negotiators and are comfortable working with OTA because it is akin to the environment in which they normally operate. Whereas the complexity of FAR can stifle input, particularly for those less experienced in working with it, working with OTA can lead to much greater levels of, and more effective, communication, which ultimately can lead to more successful projects.

Given the level of expertise from industry when negotiating under OTA, Paragas suggested that government needs to bring a similar level of expertise to the table. He noted that it is important to level the playing field and bring in the expertise and build the teams able to communicate to industry and other partners in a language that they already understand and speak on a daily basis. "It will require the government to be thinking in a different way than just bringing in a series of [General Schedule] employees." Paragas added that additional expenditures associated with building government expertise are justified in his view.

The people engaged in a negotiation need to be familiar with the "OTA roadmap." The instrument is not often used and has implications for the establishment of timelines, the approvals that are needed, when money will become available, and so on. High levels of expertise in negotiating a contract benefit both sides. The government can secure more value and be a more reliable partner. A company also can make money while serving as a reliable partner for a government agency. Paragas concluded his remarks by encouraging a refocus or reorientation to think of deployment of OTA as "taking a series of shots on goal." Investments that are not made from a cross-portfolio, programmatic vantage will not have critical mass or leverage to achieve success.

COLLABORATION AT THE CHDI FOUNDATION[7]

Robi Blumenstein, President, CHDI Management, commented that he runs a medical research foundation that does hundreds of agreements essentially under a structure akin to OTA. CHDI operates as a not-for-profit virtual organization, collaborating with and supporting a worldwide network of nearly 500 scientists in academic and industrial laboratories. Its activities extend from exploratory biology to the identification and validation of therapeutic targets, and from drug discovery and development to clinical studies and trials. CHDI also organizes workshops and meetings and makes reagents and other research tools available to the Huntington's disease research community.

The CHDI Foundation has the advantage of working on a single,

[7] This section is based on remarks given by Robi Blumenstein, President, CHDI Management.

focused disease and having access to very generous private donors so that it does not have to raise money. Under these circumstances, it is able to experiment to try to figure out how to solve problems. The foundation has a staff of about 60 people, a little more than half of whom are scientists.

On the basis of that experience, Blumenstein urged that CAN be a purposeful activity. For example, he said, collaborations need to be purposefully built through deliberate structuring of incentives. Collaborative activities can provide for fantastic leverage. But in the life sciences, people self-select into the sectors that appeal to them, Blumenstein said. People who do not mind having a boss might go into industry, while people who do not want to have a boss go into academic research. Blumenstein noted that it will be important to bring together the people who have self-selected into the different approaches, as it will take all kinds to work on the problems that need to be solved.

Finally, like Ulrey, Blumenstein lauded the idea of gathering all of the principals involved in the negotiation of a contract and working through issues together. What are the areas of overlapping interests? Where are the conflicts? Where do opportunities for mutual wins occur?

5

Situating CAN Within the Drug Development Ecosystem

Key Messages[a]

- CAN is differentiated from other entities in the drug development ecosystem, which provides it with unique opportunities.
- CAN's interactions with FDA will be an important determinant of its success.
- Possible tasks include helping to develop a regulatory science toolbox and working with industry to facilitate regulatory science to support the regulatory approval process.
- CAN could contribute to the development of a drug development ecosystem "master plan" that would establish the vision for the system, science, and tools that are needed.
- CAN could capitalize on its unique structure and function while working to advance cures alongside existing organizations and partnerships. Public–private partnerships could be a model for CAN, particularly in regard to diversity of participants and engagement in cross-sectoral training.
- Because CAN will have projects that are in the competitive product development space, issues such as conflict of interest, antitrust, confidentiality, data access, publication, and intellectual property will need to be addressed through policies.

[a] Identified by individual speakers.

CAN is part of a much larger system engaged in or supporting the development of new cures. Throughout the workshop, participants referred to this system as an "ecosystem" in which each part is shaped by, and dependent on, other parts. Even though CAN is currently small, it can influence this much larger system if it is both catalytic and strategic. And if it is successful, it can be expected to grow.

The penultimate session of the workshop featured presentations and panel discussions among participants from a variety of organizations commenting on the role of CAN within the drug development ecosystem. The session was chaired by Margaret Anderson, FasterCures, who also moderated the first panel, which explored regulatory science priorities that are important for drug development. Myrl Weinberg, President, National Health Council, moderated the second panel, which considered the role of CAN in advancing cross-sector and other collaborative translational science activities. This chapter provides an integrated summary of the presentations and panel discussions, organizing the remarks by sector to offer a multifaceted perspective on CAN's role in the drug development ecosystem and future.

FDA

FDA Regulatory Science

CAN's authorizing legislation provides that one of its functions is to "facilitate review in the Food and Drug Administration for the high need cures funded by CAN" (see Appendix B). CAN is well positioned to support such collaboration, said Jesse Goodman, Chief Scientist, FDA. It could, as an explicit part of its work, address gaps in regulatory science that, if they were filled, could greatly improve product development. In the process, CAN could help develop a regulatory science toolbox that could create a more efficient pathway to develop and evaluate products. For example, Goodman noted, there is a need for end-to-end project management and support. Innovators often do not have experience managing projects or running businesses. He suggested that it could be very helpful if NIH and CAN could provide these kinds of services or connections.

In 2011, FDA issued a regulatory science plan that also addresses gaps and opportunities in the science and in product development (FDA, 2011). Though it is a high-level plan, according to Goodman, it also lists specific areas where targeted work could accelerate the development of needed products. The report lists several FDA priority areas that are relevant to CAN:

- Modernize toxicology to enhance safety.
- Stimulate innovation in clinical evaluation and personalized medicine.
- Support new approaches to improve product manufacturing and quality.
- Ensure readiness to evaluate emerging technologies.
- Harness diverse data through information sciences to improve health outcomes.
- Facilitate development of medical countermeasures to protect U.S. and global health and security.
- Strengthen social and behavioral science to help consumers and professionals make informed decisions.

Basic science will continue to be important to develop cures for diseases, said Goodman, but so will such steps as building precompetitive cross-cutting consortia, developing better evaluative tools and measures, and supporting relevant data-gathering and data-sharing initiatives. CAN could stimulate such opportunities through project design and evaluation criteria in areas such as toxicology or Alzheimer's disease.

The Big Picture

Goodman also addressed some of the big picture issues that CAN faces. Can the program find a "sweet spot" where industry is not investing, but promising opportunities exist, thus catalyzing other interests? Perhaps such spots are characterized by higher risks, occur earlier in the development process, require new collaborations, or would benefit multiple diseases rather than a specific disease. Goodman encouraged thinking about how incentives could be created that might be missing in the commercial market to drive the timely development of needed products, including consideration of whether CAN could pick where success would have follow-on benefits in a much broader domain.

These and other projects supported by CAN require not just a scientific motivation but a business and management plan with timelines and deliverables, according to Goodman. For that reason, he proposed broadening the evaluation criteria and evaluators beyond the typical study section model. Scientific excellence must be ensured, but evaluators also could include clinicians, business people, and patients.

Management teams should have multidisciplinary representation, and projects should undergo periodic independent review by people who are not deeply invested in the project and have the authority to advise that a project be terminated or changed, Goodman said. "A lot of this is about focusing not just on what the grantees will do but how they plan to do it."

The investment made in CAN could be uniquely valuable, Goodman concluded. New values, management approaches, and team organization, combined with new tools, methods, and public knowledge, could produce tremendous benefits. Goodman noted the importance of FDA's commitment to working with CAN and its partners in the broader ecosystem.

Specific Proposals

Goodman suggested several specific potential projects for CAN related to regulatory science:

- *Develop new approaches to clinical studies.* An emphasis on relevant populations, comparator arms, and clinically meaningful outcomes, such as survival, quality of life, and patient-reported outcomes, could both help products get approved and educate physicians and patients about those products. A stronger clinical trials infrastructure and support for the development of relevant biomarkers also could enhance clinical trials, perhaps through systematic leveraging of the CTSAs.
- *Data creation and sharing.* Strong natural history data are often lacking today and could greatly help in the design of studies. Data from related products and studies could be leveraged. And some data generated in the process of product development could contribute to the field and help patients even if the product fails.
- *Early, continuous engagement of industry with FDA.* Product development pathways need to specify the indication and the anticipated risks. Scientific uncertainties can throw off a project for 2 to 3 years, and energy devoted up front to anticipating those uncertainties can be a valuable investment. Engaging with industry is resource intensive for FDA. Perhaps FDA and NIH staff or fellows could work together with grantees to extend FDA's ability to do this work, Goodman said.

Drug Development Needs

ShaAvhrée Buckman-Garner, Director, Office of Translational Sciences, Center for Drug Evaluation and Research (CDER), FDA, addressed CDER's efforts to support drug development. In 2011, CDER approved 30 new molecular entities, the highest total of new molecular entities approved in 7 years. Of those 30 new molecular entities, 12 were first in class, 11 were orphan drugs, and 19 were approved first in the United States.

The key issues have become more apparent. The development of evaluative tools is a tremendously neglected area. Better science is needed both to predict and to assess the safety and efficacy of investigational products. The major causes of failure in Phase 3 clinical development are a lack of effectiveness compared with a placebo or active control, unexpected drug toxicities, and commercial nonviability because a new therapy is no better than an existing therapy. While a large amount of biochemical and molecular knowledge may exist, there are few ways to assess the state of a whole organism or the impact of interventions at an organismal level. In addition, most assessment tools are not standardized, so the ability to compare one experiment against another is limited. The sources of variability in treatment response are largely unknown, even with current therapies. As a result, most clinical development programs are brute force empirical efforts that are extremely costly and time-consuming.

To predict, measure, and improve efficacy, major advances are needed, including new endpoints, new trial designs, better biomarkers to divide diseases into subsets according to prognostic or response predictors, patient-reported outcomes that have credibility, and natural history studies to understand disease course, particularly for rare diseases. These are "great concepts," said Buckman-Garner, but no one organization has the job of developing these ideas.

CDER has been engaging in a wide variety of collaborative efforts to help translate these concepts into action. The goal is to pull together key stakeholders, whether in academia, industry, or government, with strong project management and specific goals to ascertain the key questions and potential approaches to resolve the problems.

Medical Devices

Elizabeth Mansfield, Director of Personalized Medicine, Office of In Vitro Diagnostic Device Evaluation and Safety, Center for Devices and Radiological Health (CDRH), FDA, spoke to the relevance of CAN for medical device development. Diagnostic devices, in particular, feed drug development, approval, and use, but this area often gets short shrift in terms of funding and attention. Many developers of these devices are small companies run by people with little regulatory experience.

CDRH is increasingly working with the centers for drugs and for biologics on companion diagnostics, and "we want to be able to feed that as fast as it can go." Some drugs and biologics work well in a subset of the population, but without available diagnostics, there is no way of identifying this subset.

A Role for CAN

Given FDA's interest in trial designs, drug development tools, and modeling, Buckman-Garner pointed to four specific areas where CAN could play a very helpful role: data standards, data sharing, training, and clinical trial networks.

- *Data standards.* FDA serves as a huge repository of data, but it is not in a standardized format. Greater uniformity in the representation of data, both in case report forms and disease-specific domains, higher levels of quality, increased interoperability, and more collaboration on international standards all require a much more focused effort.
- *Data sharing.* The consortia with which FDA is involved have been seeking to facilitate precompetitive sharing of data and reduce barriers to access relevant information. As an example, Buckman-Garner cited a collaborative database of tens of thousands of electrocardiograms. However, because FDA does not own the data, only a portion of the warehouse is open for research purposes, and sponsors have to be asked before using other data. "This is a big challenge [and] just one example of the challenges that we deal with."
- *Training.* Creating an integrated workforce for translational science requires professionals skilled in clinical investigation, drug development, regulatory science, medical informatics and computer science, statistics, and other fields. Today, unmet needs exist in many of these areas, said Buckman-Garner.
- *Development of robust clinical trial networks.* Buckman-Garner noted that this effort requires the establishment of hubs for clinical trial networks that incorporate medical practitioners and also have the capacity for integration of sophisticated bench science.
- *Devices.* Mansfield added that CAN could support the development of devices by helping to build a fundamental understanding of how to translate a good idea into a product that is well understood. Many wonderful ideas emerging from NIH research, such as next-generation sequencing, will not automatically leap the chasm to become useful products unless more people know how to convert this knowledge into the needed tools. One challenge with devices is that their life cycles are extremely short compared to drugs. A device can evolve into the next-generation device within just a few years, making it difficult for FDA to predict the questions that will need to be answered. In this regard, CAN could act as a sentinel, said Mansfield, preparing the expertise and knowledge needed to expedite this process. CAN could help develop the knowledge of

how to steer a good idea through a complex regulatory process to a marketable product.

To drive CAN's investments, Buckman-Garner suggested identifying key decision points in the drug development process and prioritizing related knowledge gaps to determine

- the low-hanging fruit,
- areas of unmet needs that other consortia are not currently focusing on,
- ways to partner, and
- ways to leverage current efforts for further success.

Role of the CAN Board

Douglas Throckmorton, Deputy Director, Regulatory Programs, CDER, noted that CAN's relationship with FDA will be pivotal given FDA's prominence in CAN's authorizing legislation. Furthermore, their goals are aligned, since both organizations emphasize the development of products that are efficiently used and effective in delivering benefits.

Throckmorton also remarked on the number of disease advocates that will be on the CAN Board—as many as one-third. This is "spectacularly the right thing to do," he said. These are committed and sophisticated groups that have gone beyond getting money and providing grants to engage in careful management of ongoing efforts in an area. Patient advocacy groups straddle the public and private sectors in a productive way and, through translation or communication between these sectors, can make the CAN Board very effective.

The CAN Board can do prioritization and management, he said. It also can decide more specifically what the goals of CAN should be. It can foster communication among sectors, since each sector has less than a full understanding of the others. Finally, it can resolve misunderstandings among groups.

THE OFFICE OF SCIENCE AND TECHNOLOGY POLICY[1]

Thomas Kalil, Deputy Director for Policy, Office of Science and Technology Policy, Executive Office of the President, said that, according to an analysis by Warburg Pincus, venture capital returns on investments in the life sciences are only around 1 percent. He commented that "limited

[1] This section is based on the presentation by Thomas Kalil, Deputy Director for Policy, Office of Science and Technology Policy, Executive Office of the President.

partners are not going to be lined up around the block to invest in something that is generating a 1 percent return."

DARPA has been a model for CAN, as demonstrated by the legislative direction to use OTA. But OTA is only a small piece of what makes DARPA successful, according to Kalil. Another major element is DARPA's ability to attract world-class program managers who are the peers of the best researchers and innovators in the field. These managers are "willing to swing for the fences," said Kalil, whether that means developing a Mach 20 aircraft or prosthetics that would allow a veteran to play the piano again. Such program managers focus on specific goals rather than simply funding projects with the highest-priority scores up to the pay line. They integrate across disciplines rather than following the lead of study sections organized around disciplinary lines. They actively manage programs and are willing to support technology development even if it is not hypothesis driven.

NCATS, CAN, and NIH as a whole should invest at least a fraction of their resources according to such a model, said Kalil. DoD invests about $12 billion in R&D, and of that, $3 billion is invested in the DARPA model. "I am not suggesting that NIH invest a quarter of its resources in the DARPA approach, but I think it should be some fraction where that approach makes sense," Kalil said.

CAN also needs to invest in things that are not high-risk and high-return but that build a strong infrastructure. For example, figuring out an XML schema for case-reporting formats does not require a DARPA approach, but the argument can be made that it is important.

Kalil agreed that CAN needs to have some early wins to build congressional support. In particular, moving the needle on costs or success rates would be "the strongest argument for continuing investment." However, CAN will need to grow from the current funding levels of $10 million before it could be expected to have a major impact.

THE PHARMACEUTICAL INDUSTRY

Garry Neil, Corporate Vice President, Science and Technology, Johnson & Johnson, addressed trouble in the pharmaceutical industry. With the cost of getting a single new drug to market approaching $4 billion by some estimates, industry is highly motivated to do what it can to boost productivity in the drug development ecosystem. It knows that many stakeholders are depending on industry and counting on companies to succeed not just in getting new products into the market but in saving lives, improving quality of life, and providing cost-effective access to drugs to the maximum number of people.

Neil had the following specific suggestions for what CAN could contribute to the drug development ecosystem:

- *Help define and clarify clinical endpoints.* In the past, researchers have largely tried to adapt clinical measures of diagnosis to treatment effect, and, not surprisingly, many of these measures lack sensitivity, specificity, or validity. In addition, an imperfect disease taxonomy is driven by the same clinical markers, the population is heterogeneous, and the clinical measures of diagnosis occur late in the process because the disease is driven by clinical manifestations.
- *Contribute to target identification and validation.* Good targets linked to well-established clinical data remain scarce, which limits progress.
- *Outreach to patients and patient communities for participation in clinical trials.* Only a few percent of cancer patients who are eligible enroll in clinical trials.
- *Help advance regulatory science.* Drugs need to get into the hands of physicians and patients faster while not exposing people to unnecessary risk. At the same time, potential risks and potential benefits need to be balanced. For example, it could be helpful to reframe the question of benefit–risk to ask: what are the risks of *not* treating an individual or a group that could benefit from a new therapy?
- *Industry–FDA engagement.* Could large meetings be replaced with one-on-one engagement? Could a help desk provide information with less strain on resources? If more meetings add value, then FDA needs more resources through extension of the Prescription Drug User Fee Act or some other means.
- *Postmarketing surveillance.* It is critical to be able to adequately monitor in real time what is going on after a drug is approved and is out into the marketplace. Physicians tend to use some products quite differently than expected once they are available. Various projects are under way to monitor how products are used, but bigger investments in these areas are needed.
- *Precompetitive research.* In many areas, industry can collaborate on precompetitive research because there is no competitive advantage in owning this knowledge.

A Master Plan for Cures Acceleration

Freda Lewis-Hall, Chief Medical Officer, Pfizer Inc., also commented on CAN's role from an industry perspective. She suggested that CAN contribute to the development of a "master plan" for the drug development ecosystem that would establish the vision for the system, science, and tools that are needed. Through its master plan, CAN could systemati-

cally identify the highest-priority needs and barriers and then establish a strategy to tackle them in a coordinated way.

Lewis-Hall suggested thinking about four specific areas of opportunity that CAN could advance, as follows:

- CAN could serve as a project manager to conduct the various players, through encouragement, dissemination of best practices and worked examples, and education about opportunities to advance the field.
- CAN has the opportunity to facilitate harmonization of standards and best practices, for example, in the area of data management.
- CAN could help connect people who are working in the same area, by facilitating networking, matchmaking, communication, and sharing.
- CAN's limited funds preclude its being able to tackle all of the problems confronting the drug development ecosystem. However, CAN has the opportunity to catalyze work through provision of seed funding and following on by, for example, helping to create a foundation or other group that would be resourced to extend the work.

PUBLIC–PRIVATE PARTNERSHIPS

Public–private partnerships need to serve patients, said Ellen Sigal, Chairperson and Founder, Friends of Cancer Research. Patients want treatments that work for them and that are safe and effective. A great advantage of CAN, she said, is that it is differentiated from the other entities in the ecosystem, which provides it with unique opportunities.

Entities that have complementary missions to CAN include FNIH, the Reagan-Udall Foundation for the FDA, and the Patient-Centered Outcomes Research Institute (PCORI). FNIH has evolved over the past decade and a half. It started with small important projects and now is doing very large important projects. Reagan-Udall shares the same mission as FNIH, but for FDA. Initial funding difficulties for the organization are being resolved. PCORI is the newest entity and has substantial funding, but it will only be successful, said Sigal, if it answers questions that are important to patients.

Sigal briefly described several lessons learned from her experience. Public–private partnerships work well when they answer important questions, but they also go to the same sources for support over and over. The pharmaceutical industry has been generous, but other resources are needed. Companies' resources are limited, said Sigal, and "they have to work on the things that are most interesting to them."

Public–private partnerships are nimble and can do things that government cannot. They are not constrained by personnel or contractual issues to the same extent. They need to retain this ability to do things quickly and get nontraditional groups together and not start to act more like government.

Public–private partnerships need to have a training component for new partners, Sigal observed. For example, training programs can help patient representatives be more effective and also have the effect of bringing in new people rather than using the same people repeatedly.

CAN could do things that others are not doing by working with existing foundations, partnerships, companies, agencies, and other parts of the drug development ecosystem.

The Critical Path Institute

The Critical Path Institute (C-Path) is a public–private partnership that works with FDA to accelerate the development and review of medical products. Over the past 6 years, it has built 6 global consortia with 41 biomedical companies and more than 1,000 scientists to create tools for drug development and advance regulatory science. But it has not been easy, according to Carolyn Compton, President and Chief Executive Officer, C-Path. The collaborations require extensive multidisciplinary teams of engineers, molecular biologists, health care providers, information technology experts, project managers, and many others. Among those who participate on multiple consortia, "consortium fatigue" can be a problem.

With its partners, C-Path has brought some of the first biomarkers through the qualification process with FDA. This process of qualification improves the conversation among industry, academia, and FDA and could be supported by CAN, Compton suggested. Like Goodman, Compton also suggested that CAN contribute to the development of standards in such areas as the qualification of biomarkers, patient-recorded outcomes, and data sharing.

Compton referenced Sematech, which brought together 14 semiconductor companies to do precompetitive research in response to the perceived threat to the U.S. semiconductor industry. The first thing Sematech did, she said, was to gather metrics from the participating companies to form standards. As applied to the case of drug development, standards could be formed with regulatory decisions in mind—for example, by requiring their use in the CTSAs. Standards also could improve the end product by combining data to create a better product. And because FDA would be part of the development process, industry could be confident that the data collected for regulatory submissions could meet FDA's needs.

"I would submit that the real cool tools are the fundamental tools that support standards," said Compton. "This is an opportunity to change the culture."

The Biomarkers Consortium

The Biomarkers Consortium within FNIH identifies, develops, funds, and executes projects designed to develop and qualify biomarkers that can improve either drug development or clinical care. It is supported by the private sector, nonprofits, and NIH. It has launched 14 projects and has completed 3 of them. As an example of a recent success, David Wholley, Manager, The Biomarkers Consortium, FNIH, mentioned the establishment of new endpoints for clinical trials of community-acquired bacterial pneumonia and acute skin infections so that FDA can continue to approve new anti-infectives in these diseases.

Wholley suggested that The Biomarkers Consortium could be a model for NCATS and for CAN because of its diverse representation from all sectors of the drug development ecosystem. Steering committees and an executive committee design and then oversee the management of projects. Furthermore, all stakeholders are represented in all levels of this infrastructure. "We are able to bring the right expertise at the right time to the projects," said Wholley. "We believe you can put the 15 to 20 smartest people in a given disease area in the room, provided you have this representation, and they can come up with good ideas."

The projects take 6 to 18 months to develop and run for anywhere from 6 months to 5 years. The consortium raises funds from industry, and NIH can make parallel investments. The consortium can contribute funds directly to an NIH institute that then manages the project, but the majority of the portfolio is managed directly within FNIH.

Wholley also offered some lessons learned from his experience. He offered the opinion that Sematech is not a good model for this work. The semiconductor industry has a vertically integrated R&D system and is not a regulated industry. The challenges in drug development are "much deeper," he said.

Interactions of scientists from industry, NIH, and FDA can produce cultural change. Even small interactions have a ripple effect and can make a difference.

Wholley also mentioned possible conflicts. NIH asked that The Biomarkers Consortium be precompetitive. CAN is allowed to do some things that are in the competitive product development space, but that will raise such issues as conflict of interest, antitrust, confidentiality, data access, publication, and intellectual property. Policies at NCATS and CAN will be needed to deal with these issues.

Another issue is global harmonization. Pharmaceutical companies are global entities. The regulatory environment includes not only FDA but agencies in other countries and regions, and working with these agencies introduces an additional complication in drug development.

Finally, given the tight limits on resources, CAN will need a clear focus, and all sectors will need to be represented from the beginning. He said there is a role for third parties to work with CAN, which could extend the funding available. Public–private partnerships could leverage not just the money but the resources from across sectors.

The Reagan-Udall Foundation for the FDA

Jane Reese-Coulbourne, Executive Director, Reagan-Udall Foundation for the FDA, described projects that the Reagan-Udall Foundation has up and running and others in the works. Examples include an evaluation of multidrug tuberculosis regimens, cardiotoxicity in cancer drugs, and the reformulation of pediatric drugs.

Public–private partnerships are essential, said Reese-Coulbourne. The question is not whether to do them but how. But the members of a partnership often speak different languages, whether because they represent different scientific disciplines or different parts of the ecosystem. They also have different reward systems, which affect such issues as the sharing of data. Cultural barriers do not necessarily need to be broken down but they do need to be worked through. One way to break down these barriers is through cross-sectoral training, she said. For example, the National Breast Cancer Coalition trains not just advocates slated to serve on panels, but also scientists to understand why the advocates are there, so that information flows in both directions. Also, scientists teach some of the classes to advocates, partly to convey an understanding of scientific terminology and also to discuss and model effective behaviors in advisory roles.

CAN is designed to produce revolutionary advances, Reese-Coulbourne noted. But many existing public–private partnerships rely on old systems, not revolutionary systems. They try to do faster and harder what people have already been doing, rather than looking at the system as a whole. CAN has the opportunity not only to solve specific problems but, also to address systemic issues that are at the root of problems. It can map out the system and its problems and figure out how the parts of the system can work together to meet the needs that exist.

TOOLS AND CURES

Panelists and workshop participants discussed the goals of CAN. Sudip Parikh, Battelle Memorial Institute, expressed his opinion that Con-

gress will not take the view that development of "cool tools" should be seen as a metric of success for CAN. It would be a success for NCATS, but for CAN, he said, "the success is cures, treatments, devices, therapies, behavioral interventions." Goodman noted that he sees CAN's responsibilities as including an examination of the process for product development so that CAN advances the field and not just an individual project, thus serving the public good. He noted that industry already has incentives in regard to development of cures, and it is in the scope of a federal program such as CAN to do more. Parikh added that there are areas where treatments are needed but are not being developed. Vertex Pharmaceuticals is an example of a company driven by patient advocates where there is a high need but not much interest in the pharmaceutical industry. Kristin Schneeman, Program Director, FasterCures, offered a potential semantic clarification. She suggested that CAN, as implied by its name, is *accelerating* cures, not necessarily producing them, which could be helpful in framing CAN's metrics for success.

The discussion also touched on the role that CAN could play in helping partnerships of patient advocates, small companies, and academic researchers get high need treatments through the approval process. Goodman noted that CAN could require the developer of a product to have a plan for project management and engagement with FDA. NIH could partner with another group that could provide product developers with assistance in these areas.

Buckman-Garner added that, in this regard, CDER has been involved in an exploratory data submission program, which is designed to encourage early conversations about what is needed in product development. This program has led to meetings with groups from academia, industry, and NIH to have discussions about how to get through the regulatory process.

Neil said he could think of at least half a dozen cases of high need populations with no treatment alternatives where the problems are potentially tractable based on current scientific understanding. These cases may not be commercially attractive projects, but they offer excellent case studies of whether the drug development ecosystem could work in a different way to come up with an effective, safe, small-molecule treatment for a high need population.

6

Final Reflections on Ways to Maximize the Goals of CAN

Key Messages[a]

- CAN could break the status quo by supporting individuals and companies that are outside the mainstream.
- CAN's portfolio could focus not only on cures but on transforming the process that will lead to cures.
- Personal passion and a tolerance of failure will be important components of CAN's success.
- Possible ways to define success of CAN include
  - — installation of NCATS staff with therapeutics development expertise;
  - — implementation of milestone-based contracts and increased accountability;
  - — establishment of greater collaboration and robust public–private partnerships;
  - — advancement of regulatory science and tools for drug development tools; and
  - — development of cures: new therapeutics and diagnostics.

[a] Identified by individual speakers.

As part of the final session of the workshop, several speakers and workshop participants reflected on what they had heard over the course of the previous day and a half. Their ideas were meant to be provocative and thought-provoking as stakeholders consider the implementation and future of CAN.

RESPONDING TO FRUSTRATION[1]

Joshua Boger, Vertex Pharmaceuticals, reminded the workshop participants that the legislation leading to CAN resulted from frustration with the status quo. He cautioned that CAN will be tempted to do the same thing over and over while expecting different results, which, as Albert Einstein noted, is one definition of insanity. "CAN needs to have a very low tolerance for the status quo, and frankly for consensus, which is the basis of the status quo," said Boger. It should instead search for companies, individuals, and collaborators who are outside the mainstream, he said.

The small amount of funding initially allocated to CAN is likely to force it to work on tools rather than specific diseases, Boger said. But he added that tools are best developed in the context of a specific project. "Technology is rarely the problem," he said. "We need to close the application gap." He commented that individual projects are the best way to create system change.

Boger also expressed concern about a misalignment of goals among funders. Investors do not necessarily have the goal of creating cures. In that sense, the best co-investor is often a patient group, he said, because those are the groups most closely aligned to the mission of CAN.

Finally, he reminded the workshop participants of how difficult it will be to achieve the goals of CAN. "With all due respect, [designing] a Mach 20 aircraft is easy compared to a typical drug." Ninety-nine out of 100 drug development projects fail to make a significant medical impact. CAN's portfolio therefore needs to focus not only on cures but on transforming the process that will lead to cures. Good project management is necessary but not sufficient. "Expect most projects to fail. Don't be defensive about that. Don't over promise, and therefore you won't have to fear people or the Congress. They can handle the truth."

CAN should not be used to convert academic researchers into translational scientists, Boger said. But it can increase knowledge about the constraints on either side. In this way, it can help reshape the engagement of academic investigators with translational work.

The essential ingredient of successful drug development is personal passion sustained over long periods of time, Boger said. "All successful projects fail at least once. That should be built into the process. I know of no exceptions to that rule for any successful drug. They have all failed once. If the projects are set up to weed out failures, it will weed out successes." Even spectacular failures, if done in good faith, can amount to wins. "Insist on great science, but insist on projects that can only come about through challenging the existing process."

[1] This section is based on remarks by Joshua Boger, Founder, Vertex Pharmaceuticals.

A RALLYING CRY[2]

Carol Mimura, Assistant Vice Chancellor for Intellectual Property and Industry Research Alliances, University of California, Berkeley, labeled the workshop "a rallying cry to action . . . to change the whole ecosystem that enhances human health." Challenges abound, she said, but the workshop demonstrated the existence of an energy and a commitment to collaboration to overcome them.

Many people commented during the workshop that partnerships will be an important way to overcome barriers. She said that she has been involved at Berkeley with the establishment of hundreds of collaborations with industry; the university signs more than 350 new agreements every year. Its involvement with industry has evolved to the point that it now engages in multiparty agreements with governments and industries around the world. It also stays engaged with industry farther into the translational research arena than would be the case under the traditional technology transfer model. Innovation is not a linear process, where money goes into one end of the pipeline and drugs emerge from the other. Iteration is essential to improve on the existing situation and to align goals. "Solving the grand challenges of science requires just the right mix of talent and funding and desire and passion through successive waves of innovation."

From Mimura's perspective, the typical reason why a partnership fails is because of personal egos, not the clash of institutions. Individuals need to believe that a collaboration is worthwhile and not let personal disputes get in the way of the collective good.

Mimura emphasized the point that changes anywhere in an interconnected ecosystem can drive change in the entire system. For example, very early-stage research aimed at a commercial product typically is not ready to be picked up by biotechnology companies or pharmaceutical companies. But it can be pursued by spinoff companies from universities. In that regard, institutional innovations such as new ways to raise venture capital for small start-up companies can have wide-ranging effects.

MASTERING THE DETAILS[3]

Robert O'Neill, Senior Statistical Advisor, CDER, FDA, also commented on the sense of enthusiasm that surrounds the formation of CAN. But he cautioned that the devil is in the details. Changing the culture of organizations can be very difficult, but there are ways to do it. For

[2] This section is based on remarks by Carol Mimura, Assistant Vice Chancellor for Intellectual Property and Industry Research Alliances, University of California, Berkeley.

[3] This section is based on remarks by Robert O'Neill, Senior Statistical Advisor, CDER, FDA.

example, the contracting mechanisms pioneered by DARPA were "an eye opener," he said, because they can help make things happen that would not have happened otherwise. In that regard, he said, CAN needs to have a well-structured and carefully thought-out mechanism for prioritizing demonstration projects that have widespread impacts rather than just promoting a single project.

O'Neill also pointed to the CTSAs as a resource that needs to be reexamined to see how they can support CAN's mission. To get products to patients, the developers of those products need to be familiar with regulatory processes, and outside the drug development world not many people understand these processes. Standardization on both the medical side and the regulatory side can ease this disconnect. "Without that, we are not going to be able to do all this cross-study, cross-product research," he said.

BEYOND ROCKET SCIENCE[4]

Robert Califf, Professor of Medicine, Duke University Medical Center, pointed to the immense challenge inherent in the name given to CAN, which implies that cures will be developed in a short period of time. NIH grantees have learned to be expert at claiming victory on small advances, but they are far less expert at describing diseases they have cured, he said.

Califf also agreed that biomedical science is much more complicated than rocket science. With an engineering project, contracts can be executed ahead of time and are relatively predictable, while failures are not unexpected and typically result in the provision of more time and funding. To some extent, medical devices can be developed that way, "but drugs are horrendously more complicated."

Finally, he observed that clinical trials now can cost on the order of $500 million. "You could reduce that by 50 percent per clinical trial and probably end up with better data," he contended. But, he said, FDA is sending industry the opposite signal—that it has to spend more money to hope to survive the regulatory gauntlet.

CHANGING THE CULTURE AND SHOWING DELIVERABLES[5]

Sudip Parikh, Battelle Memorial Institute, agreed that CAN has been designed to change the culture. The rest of NIH still has $30 billion to do

[4] This section is based on remarks by Robert Califf, Professor of Medicine, Duke University Medical Center.

[5] This section is based on remarks by Sudip Parikh, Vice President of Health Policy, and Managing Director, Centers for Public Health Research and Evaluation, Battelle Memorial Institute.

hypothesis-driven research. CAN is supposed to open new spaces, even at the cost of failure. "It is not about 20 different projects at half a million dollars each planting a seed. If that is what comes out at $10 million, it will be gone next year. I can guarantee it." Far better to fund a single project that would be deemed a success, he said. Parikh said that he wants to see the research enterprise funded and valued in the way that it has been for the past 50 years, but "we have to be able to show some deliverables," encompassing a range of successes from cultural change to treatments and interventions.

As an example of a cultural change, he cited the option of hiring program managers who would focus on specific diseases with a laser-like intensity. If something does not work, what other paths can a program manager take? CAN is a vehicle to figure out the next step in the path.

CAN is an embodiment of that cultural exchange. It enumerates cures, treatments, devices, those sorts of things that can be gleaned from focused activities, Parikh said. The initial funding amount may be small, but disease foundations have demonstrated that important advances can be made for relatively little money.

"THE STATUS QUO IS NOT ACCEPTABLE"[6]

Kathy Hudson, NIH, delivered closing reflections on the workshop. "The status quo is not acceptable," she began. "We are infusing that into the brains and the hearts of everybody who works with us. The question is now whether or not we can deliver on showing that CAN can cut through red tape, create culture change, and create new tools and new processes that will make a demonstrable difference."

The proper balance between developing tools and supporting specific projects remains uncertain and will need to be addressed by the CAN Board, she said. CAN needs to have a catalytic role, especially because of its limited funding, but it also has to have a disease focus. The challenge will be to pick projects that use innovations in ways that demonstrate the potential for other projects to save time and money and "ultimately get medicines out the door faster."

The procedures CAN has been following in its initial stage are very unlike traditional procedures at NIH, which will help to change the culture. CAN expects to run programs in a "DARPAesque way," Hudson said, where milestones will be met or funding will be withdrawn. In general, in its early days, CAN plans to look closely at DARPA as a

[6] This section is based on remarks by Kathy Hudson, Acting Deputy Director, NCATS, and Deputy Director for Science, Outreach, and Policy, NIH Office of the Director.

model—for example, to learn how to use OTA and to derive best practices for collaboration between the program and contract office.

In its initial year, CAN has very little money, and it has no guarantee that funding will continue in the future. "We have an important duty to make sure that these dollars are spent well," she said. She commented that the input of the workshop was extremely beneficial. "We appreciate it very much, and we hope that we will be able to make you proud as we implement this program."

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Appendix A

Workshop Agenda

Maximizing the Goals of the Cures Acceleration Network to Accelerate the Development of New Drugs and Diagnostics: An Institute of Medicine Workshop

June 4–5, 2012

National Academy of Sciences
Keck Building, Room 100
500 Fifth Street, NW
Washington, DC 20001

Background and Meeting Objectives:

Recent years have seen both extraordinary opportunity and complex challenges in pharmaceutical innovation. New biomedical technology platforms are creating novel avenues for research and new opportunities for the discovery and clinical development of innovative diagnostics and therapies. Yet despite these advances, the pathway from basic science to new therapeutics faces challenges on many fronts. The translational divide results in only a small fraction of investigational new drugs reaching FDA approval and the patients who need them. New paradigms for discovering and developing drugs are being sought to bridge the ever-widening gap between scientific discoveries and translation of those discoveries into life-changing medications. New collaborative approaches within the federal agencies, academia, and industry are directing focused attention

on the advancement of the drug development enterprise. Among these initiatives is the Cures Acceleration Network (CAN), which was originally authorized in the Patient Protection and Affordable Care Act (P.L. 111-148) and was subsequently amended by the Consolidated Appropriations Act, FY 2012 (P.L. 112-74), which moved CAN to the newly authorized National Center for Advancing Translational Sciences (NCATS).

This public workshop will consider options and opportunities to maximize the usefulness and impact of the CAN program in order to advance translational sciences. In addition to providing suggestions to NCATS, the workshop is, in part, in response to congressional interest in CAN expressed in the FY 2012 appropriations act conference report. The workshop will inform NIH/NCATS in its efforts to implement CAN and advance translational sciences, and will also inform the public, policy community, and other stakeholders as all of these parties continue to work to enhance the development and testing of therapies and diagnostics to patients. The summary will be provided to NCATS and the newly established CAN Board to help it identify ways to accelerate and expand the number of cures.

The workshop objectives are to:

- Identify and catalog potential tools, methods, and approaches that hold promise for accelerating translational science.
  - — Consideration of such promising approaches will draw from the experiences of existing activities at other federal agencies related to the goals of CAN (e.g., FDA, CDC, AHRQ).
- Discuss the authorities conferred to CAN and identify strategies for effectively using those authorities.
  - — Consideration of the CAN authorities will specifically explore the flexible research, or "other transactions," authority and will reference existing efforts in which such authority is currently applied across other federal agencies (e.g., DARPA, DTRA, BARDA).
- Explore promising models for public–private collaborations that could be strengthened or facilitated by activities under CAN.
  - — Discuss barriers to such collaborations and identify opportunities and potential solutions for moving past the identified barriers.
  - — Discuss the respective roles of multiple sectors, including, e.g., biopharma, biotech, venture capital/private equity, and patient/disease advocacy.
- Identify barriers and potential solutions to facilitate coordination of activities under CAN with the FDA regulatory review process and timelines.

JUNE 4, 2012
DAY ONE

8:30 a.m. Opening Remarks

Workshop Co-Chairs

CAROLYN COMPTON
President and Chief Executive Officer
Critical Path Institute

LOUIS DEGENNARO
Executive Vice President and Chief Mission Officer
The Leukemia & Lymphoma Society

Session I: Overview of NIH Translational Sciences and the Cures Acceleration Network

Session Objectives:

- Provide an overview of the translational science initiatives at NIH.
- Provide an overview and description of the Cures Acceleration Network program goals and authorities.

8:40 a.m. Background and Session Objectives

SUDIP PARIKH, *Session Chair*
Vice President, Health Policy
Managing Director
Centers for Public Health Research and Evaluation
Battelle Health and Life Sciences

8:45 a.m. **Keynote Address: Introduction to NCATS and Overview of Translational Science Initiatives and CAN**

TOM INSEL
Acting Director
National Center for Advancing Translational Sciences
National Institutes of Health

9:05 a.m. **Plenary Discussion: Introduction to CAN Authorities**

LILI PORTILLA
Director, Office of Strategic Alliances
National Center for Advancing Translational Sciences
National Institutes of Health

BARBARA MCGAREY
Deputy Associate General Counsel for Public Health
Office of the General Counsel
National Institutes of Health

KATHY HUDSON
Acting Deputy Director, NCATS
Deputy Director for Science, Outreach, and Policy,
NIH Office of the Director
National Institutes of Health

9:25 a.m. **Discussion with Speakers and Audience:**

- Relationship of CAN to NCATS, other NIH Institutes/Centers
- Identification of types of activities that are likely to be undertaken under CAN
- Discussion of role of CAN Board

Session II: Approaches to Accelerating Translational Science

Session Objectives:

- Through discussion of case examples and other mechanisms, identify potential approaches that hold promise for accelerating translational science, highlighting approaches that could potentially benefit from the new CAN authorities.
- Discuss and identify attributes of success stories and failures.

9:45 a.m. Background and Session Objectives

BILL CHIN, *Session Chair*
Executive Dean for Research
Harvard Medical School

9:50 a.m. **Opening Plenary: Challenges and Needs in Translational Science—Industry Perspective**

JOSHUA BOGER
Founder, Vertex Pharmaceuticals

10:10 a.m. **Opening Plenary: Challenges and Needs in Translational Science—Academic Perspective**

R. SANDERS WILLIAMS
President
The Gladstone Institutes
University of California, San Francisco

10:30 a.m. BREAK

10:45 a.m. **Brief Presentations: Product Development/ Commercialization Efforts**

JAMES BRADNER
Assistant Professor, Harvard Medical School
Instructor in Medicine, Dana-Farber Cancer Institute

STEPHEN SEILER
Founder and Chief Executive Officer
AesRx

LOUIS DEGENNARO
Executive Vice President and Chief Mission Officer
The Leukemia & Lymphoma Society

11:25 a.m. **Discussion with Speakers and Audience:**
- What are the translational science needs?
- What approaches have failed with existing authorities? What can we learn from these failures?
- What approaches/efforts could potentially benefit from new CAN authorities?

12:05 p.m. LUNCH

Session III: Application of Matching Authority

Session Objectives:

- Explore existing efforts in which the matching authority, or similar match-type requirement, is currently applied across other federal and state agencies.
- Examine benefits and advances that have been achieved through use of this authority.
- Discuss how barriers to application and use of those authorities have been overcome.

12:35 p.m. Background and Session Objectives

NANCY SUNG
Senior Program Officer
Burroughs Wellcome Fund

12:40 p.m. **Series of Brief Presentations: Application of "Matching" or Similar Authority**

MICHAEL WEINGARTEN
Director, SBIR Development Center
National Cancer Institute
National Institutes of Health

KRISTEN DOYLE
General Counsel
Cancer Prevention and Research Institute of Texas

ELLEN FEIGAL
Senior Vice President, Research & Development
California Institute for Regenerative Medicine

1:25 p.m. **Panel Discussion with "Matchers"**

JENS ECKSTEIN
President, SR One
GlaxoSmithKline

MARTIN LEHR
Osage University Partners

MICHAEL GUTCH
Managing Director
MedImmune Ventures

Issue for Discussion:
- What are the necessary conditions for the matching program to encourage and successfully de-risk investment decisions on part of matching funders?

2:00 p.m. **Discussion with Speakers and Audience**

Issues for Discussion:
- What are the lessons learned from previous experiences?
- What are the respective roles of the various sectors (e.g., biopharma/biotech, venture capital/private equity, and patient/disease advocacy)?
- What are models for public–private collaborations that could be strengthened or facilitated by the matching authority? What are the barriers and opportunities and potential solutions for moving past those barriers?

2:30 p.m. BREAK

Session IV: Application of Flexible Research Authority

Session Objectives:

- Explore existing efforts in which the flexible research (or similar) authority is currently applied across other federal agencies.
- Examine benefits and advances that have been achieved through use of these authorities.
- Discuss how barriers to application and use of those authorities have been overcome.

2:50 p.m. Background and Session Objectives

WILLIAM WARREN, *Session Chair*
Vice President, VaxDesign Campus
Sanofi Pasteur

2:55 p.m. **Series of Presentations: Agencies**

Scott Ulrey
Deputy Director, Contracts Management Office
Defense Advanced Research Projects Agency
Department of Defense

Jason Paragas
Special Assistant to the Director
Defense Threat Reduction Agency
Department of Defense

Gerald Kovacs
Director, Division of Chemical, Biological, Radiological, and Nuclear Countermeasures
Biomedical Advanced Research and Development Authority
Office of the Assistant Secretary for Preparedness and Response

Peder Maarbjerg
Assistant Director for External Coordination
Advanced Research Projects Agency–Energy (ARPA-E)
Department of Energy

4:15 p.m. **Panel Discussion with Speakers, Discussants, and Audience: Comparing Flexible Research Authority to Existing NIH Authorities**

Discussants:

Dan Wattendorf
Program Manager, Defense Sciences Office
Defense Advanced Research Projects Agency

Robi Blumenstein
President
CHDI Management

Issues for Discussion:

- How can the other transaction authority (OTA) be most effectively applied in the biomedical/life sciences space?

- What kind of science/projects should be funded under exercise of OTA? What are the attributes of a promising project or science?
- How should the research needs be defined and executed?
- What are potential barriers that could impede the successful exercise of the OTA by NCATS/CAN? How can these barriers be overcome?
- What are the conditions for success?
- What are the respective roles of the various sectors (e.g., biopharma/biotech, venture capital/private equity, and patient/disease advocacy)?
- What are models for public–private collaborations that could be strengthened or facilitated by the flexible research authority? What are the barriers and opportunities and potential solutions for moving past those barriers?

5:30 p.m. Adjourn Day One

Maximizing the Goals of the Cures Acceleration Network to Accelerate the Development of New Drugs and Diagnostics

JUNE 5, 2012
DAY TWO

8:20 a.m. Welcome and Introductions

Workshop Co-Chairs

CAROLYN COMPTON
President and Chief Executive Officer
Critical Path Institute

LOUIS DEGENNARO
Executive Vice President and Chief Mission Officer
The Leukemia & Lymphoma Society

Session V: Situating CAN Within the Drug Development Ecosystem

Session Objectives:

- Identify potential approaches to facilitate coordination of activities under CAN with FDA regulatory science initiatives and activities.
- Discuss existing activities in multiple sectors and address ways to maximize CAN impact in the drug development ecosystem.
- Explore promising models for public–private collaborations that could be strengthened or facilitated by activities under CAN. Discuss barriers to such collaborations and identify opportunities and potential solutions for moving past the identified barriers.

8:30 a.m. Background and Session Objectives

MARGARET ANDERSON, *Session Chair*
Executive Director
FasterCures

8:35 a.m. **FDA Presentations: Intersection of CAN with FDA Regulatory Science Initiatives and Activities**

JESSE GOODMAN
Chief Scientist
Food and Drug Administration

SHAAVHRÉE BUCKMAN-GARNER
Director, Office of Translational Sciences
Center for Drug Evaluation and Research
Food and Drug Administration

9:05 a.m. **Roundtable Discussion: Identification and Discussion of Regulatory Science Priorities That Are Important for Drug Development**

Panelists

SHAAVHRÉE BUCKMAN-GARNER
Director, Office of Translational Sciences
Center for Drug Evaluation and Research
Food and Drug Administration

ELIZABETH MANSFIELD
Director, Personalized Medicine, Office of In Vitro Diagnostic Device Evaluation and Safety
Center for Devices and Radiological Health
Food and Drug Administration

THOMAS KALIL
Deputy Director for Policy
Office of Science and Technology Policy
Executive Office of the President

CAROLYN COMPTON
President and Chief Executive Officer
Critical Path Institute

GARRY NEIL
Corporate Vice President, Science and Technology
Johnson & Johnson

Panel Moderator:

MARGARET ANDERSON
Executive Director
FasterCures

9:45 a.m. **Roundtable Discussion: Role of CAN in Advancing Cross-Sector and Other Collaborative Translational Science Activities**

Panelists

ELLEN SIGAL
Founder and Chair
Friends of Cancer Research

DAVID WHOLLEY
Director, Biomarkers Consortium
Foundation for the NIH

JANE REESE-COULBOURNE
Executive Director
Reagan-Udall Foundation for the FDA

FREDA LEWIS-HALL
Chief Medical Officer
Pfizer Inc.

DOUG THROCKMORTON
Deputy Director
Center for Drug Evaluation and Research

Panel Moderator:

MYRL WEINBERG
President
National Health Council

Issues for Discussion:

- Coordination of efforts across funding agencies/sources (e.g., HHS, DoD, NGOs, industry) and with other established partners in translational research activities (e.g., FNIH, Reagan-Udall Foundation, C-Path), and reduction of duplication.
- Implications of CAN for academic translational science—career paths, funding opportunities, etc.

10:30 a.m. BREAK

Session VI: Concluding Panel Discussion: Principles for Deployment of CAN Authorities

Session Objectives:

- Discuss key themes from the workshop.
- Based on workshop presentations and discussions, identify principles for deployment of CAN authorities.

10:45 a.m. Closing Discussion with Panelists and Audience: Led by Workshop Co-Chair(s)

CAROLYN COMPTON
President and Chief Executive Officer
Critical Path Institute

LOUIS DEGENNARO
Executive Vice President and Chief Mission Officer
The Leukemia & Lymphoma Society

10:50 a.m. **Presentation of Key Themes/Suggested Paths from Workshop Session Chairs**

SUDIP PARIKH, *Session I Chair*
Vice President, Health Policy
Battelle Memorial Institute

BILL CHIN, *Session II Chair*
Executive Dean for Research
Harvard Medical School

NANCY SUNG, *Session III Chair*
Senior Program Officer
Burroughs Wellcome Fund

DAN WATTENDORF, *Session IV Rapporteur*
Program Manager, Defense Sciences Office
Defense Advanced Research Projects Agency

MARGARET ANDERSON, *Session V Chair*
Executive Director
FasterCures

11:40 a.m. **Reflecting on Potential Approaches to Maximize the Goals of CAN: Panel Discussion with Session Chairs, Panelists, and Audience**

Discussants

JOSHUA BOGER
Founder, Vertex Pharmaceuticals

KATHY HUDSON
Acting Deputy Director, NCATS
Deputy Director for Science, Outreach, and Policy, NIH Office of the Director
National Institutes of Health

CAROL MIMURA
Assistant Vice Chancellor for Intellectual Property and Industry Research Alliances
University of California, Berkeley

ROBERT O'NEILL
Senior Statistical Advisor
Center for Drug Evaluation and Research
Food and Drug Administration

12:20 p.m. **Closing Observations from NCATS**

KATHY HUDSON
Acting Deputy Director, NCATS
Deputy Director for Science, Outreach, and Policy, NIH Office of the Director
National Institutes of Health

12:30 p.m. ADJOURN

Appendix B

Public Health Service Act, Title IV—National Institutes of Health

Part E—Other Agencies of NIH

Subpart 1 National Center for Advancing Translational Sciences

SEC. 480. CURES ACCELERATION NETWORK.

(a) Definitions- In this section:

(1) BIOLOGICAL PRODUCT- The term 'biological product' has the meaning given such term in section 351 of the Public Health Service Act.

(2) DRUG; DEVICE- The terms 'drug' and 'device' have the meanings given such terms in section 201 of the Federal Food, Drug, and Cosmetic Act.

(3) HIGH NEED CURE- The term 'high need cure' means a drug (as that term is defined by section 201(g)(1) of the Federal Food, Drug, and Cosmetic Act, biological product (as that term is defined by section 262(i)), or device (as that term is defined by section 201(h) of the Federal Food, Drug, and Cosmetic Act) that, in the determination of the Director of the Center--

(A) is a priority to diagnose, mitigate, prevent, or treat harm from any disease or condition; and

(B) for which the incentives of the commercial market are unlikely to result in its adequate or timely development.

(4) MEDICAL PRODUCT- The term 'medical product' means a drug, device, biological product, or product that is a combination of drugs, devices, and biological products.

(b) Establishment of the Cures Acceleration Network.—Subject to the appropriation of funds as described in subsection (g), there is established within the Center a program to be known as the Cures Acceleration Network (referred to in this section as 'CAN'), which shall--

(1) be under the direction of the Director of the Center, taking into account the recommendations of a CAN Review Board (referred to in this section as the 'Board'), described in subsection (d); and

(2) award grants and contracts to eligible entities, as described in subsection (e), to accelerate the development of high need cures, including through the development of medical products and behavioral therapies.

(c) Functions- The functions of the CAN are to--

(1) conduct and support revolutionary advances in basic research, translating scientific discoveries from bench to bedside;

(2) award grants and contracts to eligible entities to accelerate the development of high need cures;

(3) provide the resources necessary for government agencies, independent investigators, research organizations, biotechnology companies, academic research institutions, and other entities to develop high need cures;

(4) reduce the barriers between laboratory discoveries and clinical trials for new therapies; and

(5) facilitate review in the Food and Drug Administration for the high need cures funded by the
CAN, through activities that may include--

(A) the facilitation of regular and ongoing communication with the Food and Drug Administration regarding the status of activities conducted under this section;

(B) ensuring that such activities are coordinated with the approval requirements of the Food and Drug Administration, with the goal of expediting the development and approval of countermeasures and products; and

(C) connecting interested persons with additional technical assistance made available under section 565 of the Federal Food, Drug, and Cosmetic Act.

(d) CAN Board-

(1) ESTABLISHMENT- There is established a Cures Acceleration Network Review Board (referred to in this section as the 'Board'), which shall advise the Director of the Center on the conduct of the activities of the Cures Acceleration Network.

(2) MEMBERSHIP-

(A) IN GENERAL-

(i) APPOINTMENT- The Board shall be comprised of 24 members who are appointed by the Secretary and who serve at the pleasure of the Secretary.

(ii) CHAIRPERSON AND VICE CHAIRPERSON- The Secretary shall designate, from among the 24 members appointed under clause (i), one Chairperson of the Board (referred to in this section as the 'Chairperson') and one Vice Chairperson.

(B) TERMS-

(i) IN GENERAL- Each member shall be appointed to serve a 4-year term, except that any member appointed to fill a vacancy occurring prior to the expiration of the term for which the member's predecessor was appointed shall be appointed for the remainder of such term.

(ii) CONSECUTIVE APPOINTMENTS; MAXIMUM TERMS- A member may be appointed to serve not more than 3 terms on the Board, and may not serve more than 2 such terms consecutively.

(C) QUALIFICATIONS-

(i) IN GENERAL- The Secretary shall appoint individuals to the Board based solely upon the individual's established record of distinguished service in one of the areas of expertise described in clause (ii). Each individual appointed to the Board shall be of distinguished achievement and have a broad range of disciplinary interests.

(ii) EXPERTISE- The Secretary shall select individuals based upon the following requirements:

(I) For each of the fields of--

(aa) basic research;

(bb) medicine;

(cc) biopharmaceuticals;

(dd) discovery and delivery of medical products;

(ee) bioinformatics and gene therapy;

(ff) medical instrumentation; and

(gg) regulatory review and approval of medical products, the Secretary shall select at least 1 individual who is eminent in such fields.

(II) At least 4 individuals shall be recognized leaders in professional venture capital or private equity organizations and have demonstrated experience in private equity investing.

(III) At least 8 individuals shall represent disease advocacy organizations.

(3) EX-OFFICIO MEMBERS-

(A) APPOINTMENT- In addition to the 24 Board members described in paragraph (2), the Secretary shall appoint as ex-officio members of the Board--

(i) a representative of the National Institutes of Health, recommended by the Secretary of the Department of Health and Human Services;

(ii) a representative of the Office of the Assistant Secretary of Defense for Health Affairs, recommended by the Secretary of Defense;

(iii) a representative of the Office of the Under Secretary for Health for the Veterans Health Administration, recommended by the Secretary of Veterans Affairs;

(iv) a representative of the National Science Foundation, recommended by the Chair of the National Science Board; and

(v) a representative of the Food and Drug Administration, recommended by the Commissioner of Food and Drugs.

(B) TERMS- Each ex-officio member shall serve a 3-year term on the Board, except that the Chairperson may adjust the terms of the initial ex-officio members in order to provide for a staggered term of appointment for all such members.

(4) RESPONSIBILITIES OF THE BOARD AND THE DIRECTOR OF THE CENTER -

(A) RESPONSIBILITIES OF THE BOARD-

(i) IN GENERAL- The Board shall advise, and provide recommendations to, the Director of the Center with respect to--

(I) policies, programs, and procedures for carrying out the duties of the Director of the Center under this section; and

(II) significant barriers to successful translation of basic science into clinical application (including issues under the purview of other agencies and departments).

(ii) REPORT- In the case that the Board identifies a significant barrier, as described in clause (i)(II), the Board shall submit to the Secretary a report regarding such barrier.

(B) RESPONSIBILITIES OF THE DIRECTOR OF THE CENTER - With respect to each recommendation provided by the Board under subparagraph (A)(i), the Director of the Center shall respond in writing to the Board, indicating whether such Director will implement such recommendation. In the case that the Director of the Center indicates a recommendation of the Board will not be imple-

mented, such Director shall provide an explanation of the reasons for not implementing such recommendation.

(5) MEETINGS-

(A) IN GENERAL- The Board shall meet 4 times per calendar year, at the call of the Chairperson.

(B) QUORUM; REQUIREMENTS; LIMITATIONS-

(i) QUORUM- A quorum shall consist of a total of 13 members of the Board, excluding ex-officio members, with diverse representation as described in clause (iii).

(ii) CHAIRPERSON OR VICE CHAIRPERSON- Each meeting of the Board shall be attended by either the Chairperson or the Vice Chairperson.

(iii) DIVERSE REPRESENTATION- At each meeting of the Board, there shall be not less than one scientist, one representative of a disease advocacy organization, and one representative of a professional venture capital or private equity organization.

(6) COMPENSATION AND TRAVEL EXPENSES-

(A) COMPENSATION- Members shall receive compensation at a rate to be fixed by the Chairperson but not to exceed a rate equal to the daily equivalent of the annual rate of basic pay prescribed for level IV of the Executive Schedule under section 5315 of title 5, United States Code, for each day (including travel time) during which the member is engaged in the performance of the duties of the Board. All members of the Board who are officers or employees of the United States shall serve without compensation in addition to that received for their services as officers or employees of the United States.

(B) TRAVEL EXPENSES- Members of the Board shall be allowed travel expenses, including per diem in lieu of subsistence, at rates authorized for persons employed intermittently by the Federal Government under section 5703(b) of title 5, United States Code, while away from their homes or regular places of business in the performance of services for the Board.

(e) Grant Program-

(1) SUPPORTING INNOVATION- To carry out the purposes described in this section, the Director of the Center shall award contracts, grants, or cooperative agreements to the entities described in paragraph (2), to--

(A) promote innovation in technologies supporting the advanced research and development and production of high need cures, including through the development of medical products and behavioral therapies.

(B) accelerate the development of high need cures, including through the development of medical products, behavioral therapies, and biomarkers that demonstrate the safety or effectiveness of medical products; or

(C) help the award recipient establish protocols that comply with Food and Drug Administration standards and otherwise permit the recipient to meet regulatory requirements at all stages of development, manufacturing, review, approval, and safety surveillance of a medical product.

(2) ELIGIBLE ENTITIES- To receive assistance under paragraph (1), an entity shall--

(A) be a public or private entity, which may include a private or public research institution, an institution of higher education, a medical center, a biotechnology company, a pharmaceutical company, a disease advocacy organization, a patient advocacy organization, or an academic research institution;

(B) submit an application containing--

(i) a detailed description of the project for which the entity seeks such grant or contract;

(ii) a timetable for such project;

(iii) an assurance that the entity will submit--

(I) interim reports describing the entity's--

(aa) progress in carrying out the project; and

(bb) compliance with all provisions of this section and conditions of receipt of such grant or contract; and

(II) a final report at the conclusion of the grant period, describing the outcomes of the project; and

(iv) a description of the protocols the entity will follow to comply with Food and Drug Administration standards and regulatory requirements at all stages of development, manufacturing, review, approval, and safety surveillance of a medical product; and

(C) provide such additional information as the Director of the Center may require.

(3) AWARDS-

(A) THE CURES ACCELERATION PARTNERSHIP AWARDS-

(i) INITIAL AWARD AMOUNT- Each award under this subparagraph shall be not more than $15,000,000 per project for the first fiscal year for which the project is funded, which shall be payable in one payment.

(ii) FUNDING IN SUBSEQUENT FISCAL YEARS- An eligible entity receiving an award under clause (i) may apply for additional funding for such project by submitting to the Direc-

tor of the Center the information required under subparagraphs (B) and (C) of paragraph (2). The Director may fund a project of such eligible entity in an amount not to exceed $15,000,000 for a fiscal year subsequent to the initial award under clause (i).

(iii) MATCHING FUNDS- As a condition for receiving an award under this subsection, an eligible entity shall contribute to the project non-Federal funds in the amount of $1 for every $3 awarded under clauses (i) and (ii), except that the Director of the Center may waive or modify such matching requirement in any case where the Director determines that the goals and objectives of this section cannot adequately be carried out unless such requirement is waived.

(B) THE CURES ACCELERATION GRANT AWARDS-

(i) INITIAL AWARD AMOUNT- Each award under this subparagraph shall be not more than $15,000,000 per project for the first fiscal year for which the project is funded, which shall be payable in one payment.

(ii) FUNDING IN SUBSEQUENT FISCAL YEARS- An eligible entity receiving an award under clause (i) may apply for additional funding for such project by submitting to the Board the information required under subparagraphs (B) and (C) of paragraph (2). The Director of the Center may fund a project of such eligible entity in an amount not to exceed $15,000,000 for a fiscal year subsequent to the initial award under clause (i).

(C) THE CURES ACCELERATION FLEXIBLE RESEARCH AWARDS- If the Director of the Center determines that the goals and objectives of this section cannot adequately be carried out through a contract, grant, or cooperative agreement, the Director of the Center shall have flexible research authority to use other transactions to fund projects in accordance with the terms and conditions of this section. Awards made under such flexible research authority for a fiscal year shall not exceed 20 percent of the total funds appropriated under subsection (g)(1) for such fiscal year.

(4) SUSPENSION OF AWARDS FOR DEFAULTS, NONCOMPLIANCE WITH PROVISIONS AND PLANS, AND DIVERSION OF FUNDS; REPAYMENT OF FUNDS- The Director of the Center may suspend the award to any entity upon noncompliance by such entity with provisions and plans under this section or diversion of funds.

(5) AUDITS- The Director of the Center may enter into agreements with other entities to conduct periodic audits of the projects funded by grants or contracts awarded under this subsection.

(6) CLOSEOUT PROCEDURES- At the end of a grant or contract period, a recipient shall follow the closeout procedures under sec-

tion 74.71 of title 45, Code of Federal Regulations (or any successor regulation).

(7) REVIEW- A determination by the Director of the Center as to whether a drug, device, or biological product is a high need cure (for purposes of subsection (a)(3)) shall not be subject to judicial review.

(f) Competitive Basis of Awards- Any grant, cooperative agreement, or contract awarded under this section shall be awarded on a competitive basis.

(g) Authorization of Appropriations-

(1) IN GENERAL- For purposes of carrying out this section, there are authorized to be appropriated $500,000,000 for fiscal year 2010, and such sums as may be necessary for subsequent fiscal years. Funds appropriated under this section shall be available until expended.

(2) LIMITATION ON USE OF FUNDS OTHERWISE APPROPRIATED- No funds appropriated under this Act, other than funds appropriated under paragraph (1), may be allocated to the Cures Acceleration Network.

Appendix C

Participant Biographies

Carolyn Compton, M.D., Ph.D. (*Workshop Co-Chair*), is the President and CEO of C-Path. She was most recently the Director of the Office of Biorepositories and Biospecimen Research (OBBR) and the Executive Director of the Cancer Human Biobank (caHUB) project at NCI. In these capacities, she had leadership responsibility for strategic initiatives that included the Innovative Molecular Analysis Technologies for Cancer program, the Biospecimen Research Network program, and the NCI Community Cancer Centers project. She is an adjunct professor of pathology at the Johns Hopkins School of Medicine. She received her M.D. and Ph.D. degrees from Harvard Medical School and the Harvard Graduate School of Arts and Sciences. She trained in pathology at Harvard's Brigham and Women's Hospital and is boarded in both anatomic pathology and clinical pathology. She came to NCI from McGill University, where she had been the Strathcona Professor and Chair of Pathology and the Pathologist-in-Chief of McGill University Health Center from 2000 to 2005. Prior to this, she had been a professor of pathology at Harvard Medical School, the Director of Gastrointestinal Pathology at Massachusetts General Hospital, and the Pathologist-in-Chief of the Shriners Hospital for Crippled Children, Boston Burns Unit, for 15 years. During this time she served as Chair of the Pathology Committee of the Cancer and Leukemia Group B for 12 years. Her research interests are in colon and pancreatic cancer as well as epithelial biology and wound healing. Dr. Compton has held many national and international leadership positions in pathology and cancer-related professional organizations. She is a Fellow of the College

of American Pathologists and a Fellow of the Royal Society of Medicine. Currently, she is the Chair of the American Joint Committee on Cancer (AJCC), serves on the Executive Committee of the Commission on Cancer of the American College of Surgeons, and serves as the Pathology Section Editor for *Cancer*. She is a past Chair of the Cancer Committee of the College of American Pathologists and was Editor of the first edition of the CAP Cancer Protocols (Reporting on Cancer Specimens) used as standards for COC accreditation. Among her awards are the ISBER Award for Outstanding Achievement in Biobanking, the NIH Director's Award, the NIH Award of Merit, and the CAP Frank W. Hartman Award. She has published more than 500 original scientific papers, reports, review articles, books, and abstracts.

Louis J. DeGennaro, Ph.D. (*Workshop Co-Chair*), is Executive Vice President and Chief Mission Officer, LLS. As Chief Mission Officer, Dr. DeGennaro's current responsibilities include oversight of all LLS mission functions: Public Policy, Patient Services, and Research with the goal of effectively deploying resources in pursuit of the LLS mission to cure leukemia, lymphoma, and myeloma and to improve the quality of life for patients and their families. The Society's mission budget exceeds $100 million annually. Dr. DeGennaro has more than 25 years of research, drug development, and executive management experience in academic and private-sector settings. He received his Ph.D. in biochemistry from the University of California, San Francisco, and did his postdoctoral research at Yale University School of Medicine. His previous academic appointments include research group leader, Max Planck Institute in Munich, Germany, where his laboratory was among the first to clone genes expressed exclusively in the nervous system; and associate professor of neurology and cell biology, University of Massachusetts Medical School. Dr. DeGennaro's private-sector positions include senior director of molecular genetics at Wyeth Pharmaceuticals, Princeton, New Jersey, where his department contributed to the development of pantoprazole (Protonix®) to treat acid reflux disease, Effexor (Venlafaxine®) for anxiety and depression, and Mylotarg® for leukemia; executive vice president for research and development, SynX Pharma, Inc., in Toronto, Canada, where he was responsible for the development of a point-of-care diagnostic test for congestive heart failure; and research manager at Streck, Inc., Omaha, Nebraska, where he helped develop an FDA-cleared diagnostic test for AIDS/HIV.

Margaret Anderson, M.S., is Executive Director of FasterCures/The Center for Accelerating Medical Solutions, defining the organization's strategic priorities and positions on key issues, developing its programmatic portfolio, and managing its operations. Prior to her appointment as

Executive Director, she was FasterCures' COO for 5 years. Ms. Anderson previously served as deputy director of the Academy for Educational Development (AED), where she was also a team leader in the Center on AIDS & Community Health. Prior to AED, she led programs and studies at the Society for Women's Health Research, the American Public Health Association, and the Congressional Office of Technology Assessment. She currently serves on the boards of the Alliance for a Stronger FDA, the Council for American Medical Innovation, and the Coalition for the Advancement of Medical Research, and has held numerous committee and coalition memberships for federal agencies and professional associations in the biomedical and public health arena. Ms. Anderson holds a bachelor's degree from the University of Maryland and a master's degree in science, technology, and public policy from George Washington University's Elliott School of International Affairs.

Robi Blumenstein, L.L.B., M.B.A., is President of CHDI Management. Mr. Blumenstein organized CHDI Management in 2002 to provide management services to nonprofit organizations engaged in Huntington's disease research. Mr. Blumenstein began his career as a lawyer at Torys, a law firm in Toronto, before moving into merchant banking, where he was responsible for structuring and negotiating transactions and supervising investment analysis. He was a principal at First City Capital Corporation, CIBC Capital Partners, and MMC Capital. Mr. Blumenstein was a director of Life Times Nine, a short subject film that was nominated for an Academy Award in 1973. Mr. Blumenstein graduated from the University of Toronto with a B.A. (1975) and an L.L.B. (1978) and has an M.B.A. from Harvard Business School (1984).

Joshua Boger, Ph.D., is the Founder of Vertex Pharmaceuticals Incorporated (NASDAQ: VRTX). He retired as Vertex's Chief Executive Officer in May 2009, after more than 20 years with the company. He continues to serve on the Vertex Board. Prior to founding Vertex in 1989, he worked for more than a decade in pharmaceutical research at Merck, where he developed an international reputation as a leader in the application of computer modeling to the chemistry of drug design and was a pioneer in the use of structure-based rational drug design as the basis for drug discovery programs. He holds a bachelor of arts in Chemistry and Philosophy from Wesleyan University, Middletown, Connecticut, and master's and doctorate degrees in Chemistry from Harvard University. He is the author of more than 50 scientific publications; holds 32 issued U.S. patents in pharmaceutical discovery and development; and has lectured widely in the United States, Europe, and Asia on various aspects of drug discovery, development, and commercialization. Among a large number of

nonprofit affiliations, he is the Chair of the Board of Trustees at Wesleyan University, Chair of the Board of Fellows of the Harvard Medical School, Chair of NEHI (the Network for Healthcare Innovation, Cambridge), and Vice-Chair of the Boston Museum of Science.

James Bradner, M.D., is an Instructor in Medicine and Staff Physician in Hematologic Malignancies at Dana-Farber Cancer Institute, as well as an assistant professor in medicine at Harvard Medical School. The research focus of his laboratory concerns the discovery/optimization of prototype drugs targeting cancer gene regulation. Clinically, The Bradner Group strives to deliver novel therapeutics for human clinical investigation in hematologic diseases. Dr. Bradner is a member of the American Society of Clinical Investigation, the American Society of Hematology, the American Chemical Society, and the American Association of Cancer Research. His recent research has been published in *Nature*, *Cell*, *Nature Chemical Biology*, and the *Journal of the American Chemical Society*. He has authored 16 U.S. patent applications, licensed to five pharmaceutical companies, and is a scientific founder of Acetylon Pharmaceuticals, SHAPE Pharmaceuticals, and Tensha Therapeutics.

ShaAvhrée Y. Buckman-Garner, M.D., Ph.D., FAAP, is the Director of the Office of Translational Sciences (OTS), CDER, FDA. OTS is comprised of the Office of Biostatistics, Office of Clinical Pharmacology, and provides oversight to CDER research involving human subjects as well as CDER regulatory science research. OTS is responsible for providing coordination for Critical Path initiatives across CDER in partnership with individual CDER offices. OTS also provides oversight for the CDER Computational Science Center. Prior to serving as Director of OTS, Dr. Buckman-Garner served as Deputy Director for OTS and as medical team leader in the Division of Pediatric Drug Development, Office of Counter Terrorism and Pediatric Drug Development, CDER. Dr. Buckman-Garner received her M.D. and Ph.D. degrees with an emphasis on molecular cell biology from Washington University School of Medicine. Dr. Buckman-Garner completed pediatric specialty training at Baylor College of Medicine.

William W. Chin, M.D., is the Executive Dean for Research at Harvard Medical School (HMS). In this role, Dr. Chin spearheads efforts to design and implement the vision for research at HMS, with special emphasis on interdisciplinary and translational research that crosses departmental and institutional boundaries. Dr. Chin is a Harvard-trained endocrinologist and longstanding faculty member. He was professor of medicine, HMS; Chief, Division of Genetics and Senior Physician, Brigham and Women's Hospital; and Investigator, Howard Hughes Medical Institute. His impres-

sive career is exemplified in part by his extensive bibliography of nearly 300 papers, chapters, and books, most of which were generated during his 25 years at HMS. As a pioneering molecular endocrinologist at HMS, Dr. Chin embraced the early use of emerging DNA technology to make important discoveries regarding the structure, function, and regulation of hormone genes. His investigations often demonstrated a translational research theme, connecting basic laboratory discoveries to their physiologic relevance in animal models and humans. He has been honored with numerous awards for research, mentorship, and leadership. Prior to HMS, Dr. Chin was at Eli Lilly & Co., where he had worked for the past decade, most recently as senior vice president for Discovery Research and Clinical Investigation. He is a graduate of Columbia College and HMS.

Kristen Doyle, J.D., M.S.T.C., is responsible for overseeing the legal issues that arise as part of CPRIT's operations, including grant award contract negotiations, intellectual property and revenue sharing agreements, conflicts of interest and confidentiality, and regulatory/compliance issues. Prior to joining CPRIT, Ms. Doyle was a partner at an Austin-based law firm and served as Vice President of the Board of Directors for the Central Texas Chapter for LLS. Ms. Doyle has spent the majority of her legal career practicing administrative law, with an emphasis in the field of energy and regulatory law. She received her undergraduate degree in public policy, magna cum laude, from Indiana University and her doctorate of jurisprudence from the University of Texas at Austin School of Law. She has been recognized four times as a Super Lawyers Texas Rising Star by *Texas Monthly* and named to the 2010 edition of The Best Lawyers in America. She is a frequent speaker on administrative law and legislative policy issues. Ms. Doyle joined CPRIT in July 2009.

Jens Eckstein, Ph.D., comes to SR One from TVM Capital, where he was a venture partner, entrepreneur-in-residence, and appointed CEO and President of SelectX Pharmaceuticals. Prior to that, he was a general partner in TVM's Boston life sciences practice, where he focused on earlier-stage investments. He was a member of the Board of Directors for CoNCERT Pharmaceuticals, Enanta Pharmaceuticals, SelectX Pharmaceuticals, Rapid Micro Biosystems, and Anchor Therapeutics and was an advisor to Sirtris Pharmaceuticals. Dr. Eckstein was the founder of Akikoa Pharmaceuticals, a biotechnology start-up company focusing on hearing loss, and North Haven Systems, a life science IT company. Prior to joining TVM Capital, he led drug discovery programs at Enanta Pharmaceuticals, Inc., and Mitotix, Inc. He is the author of numerous scientific publications and holds several issued and pending patents. He was managing editor of *Frontiers in Biosciences* "Current Topics in Lead Discovery" and served as

an editorial board advisor for *IDrugs*. He is an advisor to the Alzheimer Research Forum (ARF), founding member of the Cure Dystonia Initiative Advisory Council (CDIAC), and a Kauffman Fellow.

Ellen G. Feigal, M.D., M.S., is the Senior Vice President, R&D at CIRM. Prior to joining CIRM in January 2011, Dr. Feigal was Executive Medical Director, Global Development, at Amgen, where her primary focus was in clinical development of therapeutics in hematology/oncology. She also led the scientific/clinical interface with patient advocacy organizations, formalized the company's policy on expanded access to therapies for those with limited or no treatment options, and led the cross-functional teams to the company's first collaborative research and development agreement with NCI. From 2007 until joining CIRM, Dr. Feigal was adjunct professor and founding Director of the American Course on Drug Development and Regulatory Sciences, University of California, San Francisco (UCSF), School of Pharmacy. The course, developed under her leadership as a collaborative effort with FDA, UCSF's Department of Bioengineering and Therapeutic Sciences, its Center for Drug Development Sciences, and the European Center of Pharmaceutical Medicine at the University of Basel, was launched in 2007. It is taught in Washington, DC, with a separate parallel course in San Francisco. Prior to joining Amgen in 2008, she worked in clinical research and drug development in positions at the federal government, nonprofit and for-profit institutes, and companies. She was Chief Medical Officer, Insys Therapeutics, from 2007 to 2008, Director of Medical Devices and Imaging at C-Path, and Vice President of Clinical Sciences and Deputy Scientific Director at the Translational Genomics Research Institute from 2004 to 2007. She directed NCI's Division of Cancer Treatment and Diagnosis from 2001 to 2004, served as Deputy Director from 1997 through 2001, and as senior investigator in the Cancer Therapy Evaluation Program, NCI, from 1992 to 1997. Dr. Feigal earned a B.S. in biology from UC Irvine, an M.S. in molecular biology and biochemistry from UC Irvine, and an M.D. from UC Davis. She completed her residency in internal medicine at Stanford University and her fellowship in hematology/oncology at UCSF. She was on the faculty at UCSF and UC San Diego before joining NCI.

Jesse L. Goodman, M.D., M.P.H., became Chief Scientist, FDA, in 2009. He has broad responsibility for and engagement in leadership and coordination of the Agency's cross-cutting scientific and public health efforts. From 2003 to 2009, he was Director of FDA's Center for Biologics Evaluation and Research (CBER), which oversees medical and public health activities critical to U.S. and global preparedness concerning the development, evaluation, safety, quality, and availability of biologics. A graduate

of Harvard, he received his M.D. from the Albert Einstein College of Medicine and did residency and fellowship training at the Hospital of the University of Pennsylvania and at UCLA (where he was also Chief Medical Resident). Prior to joining FDA, he was professor of medicine and Chief of Infectious Diseases at the University of Minnesota, where he directed the multihospital infectious diseases research, training, and clinical programs, and where his NIH-funded laboratory first isolated and characterized *Anaplasma phagocytophilum*, the infectious agent causing a new tick-borne disease, human granulocytic ehrlichiosis. He has authored numerous scientific papers and edited the book *Tick-Borne Diseases of Humans*, published by ASM Press in 2005. Dr. Goodman has been elected to the American Society for Clinical Investigation and to the IOM of the National Academy of Sciences, where he is a longstanding member of the Forum on Emerging Threats. He is an active clinician and teacher who is board-certified in internal medicine, oncology, and infectious diseases; is Staff Physician and Infectious Diseases Consultant at both the National Naval and Walter Reed Army Medical Centers; and is adjunct professor of medicine at the University of Minnesota.

Michael Gutch, Ph.D., M.B.A., had experience as both a corporate and private venture capital investor prior to joining MedImmune Ventures (MV) in September 2011. Before MV, Dr. Gutch was a Director with H.I.G. BioVentures, a life science–focused investment fund, and prior to that was a Principal with Lilly Ventures, the corporate venture capital arm of Eli Lilly & Co. While at Eli Lilly & Co., Dr. Gutch was also in the Corporate Financing and Investment Banking group, where he focused on mergers, acquisitions, and licensing transactions. Dr. Gutch earned his Ph.D. in cellular and molecular pathology from the State University of New York at Stony Brook and was a postdoctoral research fellow at both UCSF and the Cold Spring Harbor Laboratories. He earned his M.B.A. in finance from Indiana University. Dr. Gutch currently serves as a member of the Board of Directors for Southeast BIO, the Johns Hopkins Alliance for Science & Technology Development, and the Business Advisory Board for the Alzheimer's Drug Discovery Foundation.

Kathy Hudson, Ph.D., M.S., is the Deputy Director for Science, Outreach, and Policy at NIH, the world's largest biomedical research agency, with an annual budget of $31 billion. In this position, Dr. Hudson works closely with and oversees the activities of the Associate Directors for Communications and Public Liaison, Legislative Policy and Analysis, and Science Policy. In addition, Dr. Hudson works with NIH leadership to develop and implement new strategic and scientific initiatives and is the NIH liaison with the U.S. Department of Health and Human Services. She

represents the NIH—and the NIH Director—in high-level collaborations and negotiations with other federal agencies, such as FDA, CDC, and the White House Office of Science and Technology Policy, as well as with private research institutions, patient voluntary organizations, and professional societies. In December 2011, NCATS was established as a new component of NIH with a mandate to streamline the way translational research is done. At that time, Dr. Hudson was designated Acting Deputy Director of NCATS. In that role she leads the many activities of bringing the Center into being and getting its programs under way.

Thomas R. Insel, M.D., graduated from Boston University, where he received a B.A. from the College of Liberal Arts and an M.D. from the Medical School. He did his internship at Berkshire Medical Center, Pittsfield, Massachusetts, and his residency at the Langley Porter Neuropsychiatric Institute at the University of California, San Francisco. Dr. Insel joined the National Institute of Mental Health (NIMH) in 1979, where he served in various scientific research positions until 1994, when he went to Emory University, Atlanta, as professor, Department of Psychiatry, Emory University School of Medicine, and Director of the Yerkes Regional Primate Research Center. As director of Yerkes, Dr. Insel built one of the nation's leading HIV vaccine research programs. At the time of the workshop, he was the Acting Director of NCATS. He currently serves as the Founding Director of the Center for Behavioral Neuroscience, a science and technology center funded by the National Science Foundation (NSF). The Center has developed an interdisciplinary consortium for research and education at eight Atlanta colleges and universities. Dr. Insel first joined NIMH in 1979 as a clinical associate in the Clinical Neuropharmacology Branch and went on to hold several administrative and leadership posts. During his 15 years at NIMH before heading to Emory in 1994, he conducted research in obsessive-compulsive disorder (OCD), initiating some of the first treatment trials for OCD using serotonin reuptake inhibitors. Dr. Insel oversees NIMH's $1.3 billion research budget, which provides support to investigators at universities throughout the country in the areas of basic science; clinical research, including large-scale trials of new treatments; and studies of the organization and delivery of mental health services.

Thomas A. Kalil is currently serving as Deputy Director for Policy for the White House Office of Science and Technology Policy and Senior Advisor for Science, Technology and Innovation for the National Economic Council. From 2001 to 2008, Mr. Kalil was Special Assistant to the Chancellor for Science and Technology at UC Berkeley. He was respon-

sible for developing major new multidisciplinary research and education initiatives at the intersection of information technology, nanotechnology, microsystems, and biology. He also conceived and launched a program called "Big Ideas @ Berkeley," which provides support for multidisciplinary teams of Berkeley students who are interested in addressing economic and societal challenges such as clean energy, safe drinking water, and poverty alleviation. In 2007 and 2008, Mr. Kalil was the Chair of the Global Health Working Group for the Clinton Global Initiative, where he developed new public- and private-sector initiatives in areas such as maternal and child health, under-nutrition, and vaccines. Mr. Kalil was also a Senior Fellow with the Center for American Progress (CAP), where he co-authored *A National Innovation Agenda*, one of the four pillars of CAP's Economic Plan for the Next Administration. He was also a member of the Scientific Advisory Board of Nanomix and has served on three committees of the National Academy of Sciences, including the Committee to Facilitate Interdisciplinary Research. Previously, Mr. Kalil served as the Deputy Assistant to President Clinton for Technology and Economic Policy and the Deputy Director of the White House National Economic Council (NEC). He was NEC's "point person" on a wide range of technology and telecommunications issues, such as the liberalization of Cold War export controls, the allocation of spectrum for new wireless services, and investments in upgrading America's high-tech workforce. He led a number of White House technology initiatives, such as the National Nanotechnology Initiative, the Next Generation Internet, bridging the digital divide, e-learning, increasing funding for long-term information technology research, making IT more accessible to people with disabilities, and addressing the growing imbalance between support for biomedical research and for the physical sciences and engineering. He was also appointed by President Clinton to serve on the G-8 Digital Opportunity Task Force (dot force). Prior to joining the White House, Mr. Kalil was a trade specialist at the Washington offices of Dewey Ballantine, where he represented the Semiconductor Industry Association on U.S.–Japan trade issues and technology policy. He also served as the principal staffer to Gordon Moore in his capacity as Chair of the SIA Technology Committee. Mr. Kalil received a B.A. in political science and international economics from the University of Wisconsin–Madison and completed graduate work at the Fletcher School of Law and Diplomacy. He is the author of articles and op-eds on S&T policy, the use of prizes as a tool for stimulating innovation, nanotechnology, nuclear strategy, newborn health, vaccines, the impact of mobile communications in developing countries, U.S.–Japan trade negotiations, U.S.–Japan cooperation in science and technology, the National Information Infrastructure, distributed learning, and electronic commerce.

Gerald Kovacs, Ph.D., is Director of the Division of CBRN Countermeasures in the Office of BARDA in the Department of Health and Human Services Office of the Assistant Secretary for Preparedness and Response. At BARDA, Dr. Kovacs focuses on addressing the major scientific and regulatory challenges of developing medical countermeasures (vaccines, therapeutics, and diagnostics) against CBRN threats. Dr. Kovacs is responsible for the development, implementation, and oversight of programs authorized by the Project BioShield Act of 2004 and the Pandemic and All Hazards Preparedness Act of 2006. Since joining BARDA in 2005, Dr. Kovacs has expanded BARDA's portfolio of CBRN programs from 4 to more than 60. He has led five candidates through Phase 2 clinical testing and has delivered five first-in-class medical countermeasures to the Strategic National Stockpile. From 2003 to 2005, Dr. Kovacs was instrumental in establishing the Office of Biodefense Research Affairs (OBRA) at the National Institute of Allergy and Infectious Diseases. At OBRA, he formed the team that developed a novel smallpox vaccine for use in immune-compromised individuals. He completed clinical studies in healthy, atopic, and HIV-infected subjects, and delivered more than 1 million doses of vaccine to the U.S. government. Prior to his career in public service, Dr. Kovacs was a principal research scientist at Wyeth Vaccines. During that period, he led programs in herpes simplex, arainfluenza, respiratory syncytial, and papilloma virus vaccine development. He also led Wyeth's post–9/11 efforts in the development of a second-generation smallpox vaccine. Dr. Kovacs received his doctorate degree from the Department of Biochemistry and Biophysics at Texas A&M University and subsequently trained as a postdoctoral fellow at Harvard Medical School and NIH. He is also a graduate of the Federal Executive Institute.

Martin Lehr, M.A., joined Osage University Partners in 2009 and focuses on novel biopharmaceutical products, medical devices, diagnostics, and research tools. Prior to joining Osage, Mr. Lehr conducted research in the areas of DNA repair at the Sloan-Kettering Institute and in thrombin activation at the Children's Hospital of Philadelphia. Mr. Lehr is on the Advisory Board of the Sid Martin Biotech Incubator at the University of Florida, is an advisor to the University City Science Center's QED Program, and is a mentor to the University of Pennsylvania's Life Science Management program. He serves as Secretary of the BioBreak organization and is an organizer of Philly BioBreak, a group dedicated to fostering a thriving life science community in the Greater Philadelphia Area. Mr. Lehr holds an M.A. in biotechnology from Columbia University and a B.A. in economics from the University of Pennsylvania.

Freda C. Lewis-Hall, M.D., has been appointed Chief Medical Officer and Senior Vice President, Pfizer Inc. Dr. Lewis-Hall will be the senior physician in the company, responsible for enterprise-wide medical, patient safety, regulatory affairs, and quality assurance as well as outreach to doctors and other medical professionals. Dr. Lewis-Hall will report to Mr. Kindler and serve on Pfizer's Executive Leadership Team, its most senior leadership group. She will shape Pfizer's regulatory and medical policy during a time of fast-changing expectations for health care companies and a wave of new therapies in development, especially as information technologies change the ways companies develop medicines, clinicians prescribe them, and patients and payers value them. Prior to joining Pfizer, Dr. Lewis-Hall was Executive Vice President, Medicines Development of Vertex Pharmaceuticals, where she was responsible for clinical and nonclinical development as well as both medical and regulatory development; she also served as Senior Vice President of Medical Affairs at Bristol-Myers Squibb; Vice President of Research and Development at Pharmacia; and Product Team Leader at Eli Lilly & Co. Dr. Lewis-Hall is a Fellow of the American Academy of Psychiatry. She received her bachelor of arts and sciences from Johns Hopkins University and her medical doctorate from Howard University Hospital and College of Medicine.

Peder Maarbjerg, J.D., currently serves as Assistant Director for External Coordination at ARPA-E and is responsible for legislative and public policy outreach. Prior to joining ARPA-E, Mr. Maarbjerg served as Senior Policy Fellow at the U.S. Nuclear Infrastructure Council, where he researched legislative and policy trends, with a focus on administrative law and budget policy. Previously, Mr. Maarbjerg was the Appropriations and Legislative Director for a senior member of the U.S. House of Representatives, Energy and Water Appropriations Subcommittee. He is also a member of the Federal Energy Bar. Mr. Maarbjerg received his B.A. in anthropology and history from Union College, New York, and his J.D. cum laude in environmental law from the University of Baltimore.

Elizabeth Mansfield, Ph.D., is Director of the Personalized Medicine Staff in the Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD), CDRH, FDA, where she is developing a program to address companion and novel diagnostic devices. She was previously a Senior Policy Analyst in OIVD, managing policy and scientific issues. Dr. Mansfield formerly served as the Director of Regulatory Affairs at Affymetrix, Inc. (2004–2006). She previously served in other positions at FDA, including Scientific Reviewer and Genetics Expert. Dr. Mansfield received her Ph.D. from Johns Hopkins University, and completed further postdoctoral training at NIH.

Barbara M. McGarey, J.D., is Deputy Associate General Counsel for Public Health, NIH Office of the General Counsel (OGC), U.S. Department of Health and Human Services. Ms. McGarey serves as chief counsel for NIH in Bethesda, Maryland, and supervises the NIH Branch of the Public Health Division, OGC. The NIH Branch is the in-house counsel to NIH, providing legal advice on NIH research, policy development, grants and contracts, patents, and hospital and other facility operations. Ms. McGarey has served in this capacity since September 2001. Ms. McGarey has extensive knowledge and experience on the funding and regulation of biomedical research, with an emphasis on intellectual property law. Her prior positions include General Counsel to the NIH Foundation (2000–2001), Deputy Director of the NIH Office of Technology Transfer (1993–2000), and staff attorney and Acting Branch Chief in the Public Health Division, OGC (1987–1993). She began her legal career through the Honors Program at the U.S. Department of Justice in the Civil Division, Office of Consumer Litigation (1985–1987). Ms. McGarey graduated with honors from Catholic University Law School in 1985, where she served on the *Catholic University Law Review* staff and was a founding co-editor of the *Journal of Contemporary Health Law*. Prior to law school, Ms. McGarey received a bachelor of science from Cornell University, and worked as a cardiac surgery intensive care unit nurse.

Carol Mimura, Ph.D., is Assistant Vice Chancellor for Intellectual Property and Industry Research Alliances (IPIRA) at the University of California, Berkeley (UC Berkeley). IPIRA is the portal to Berkeley for industry access to Berkeley's preeminent faculty and research capabilities. Dr. Mimura has a bachelor of science degree from Yale University in molecular biophysics and biochemistry and a Ph.D. in biology (biochemistry and microbiology concentration) from Boston University. She was an NIH-sponsored postdoctoral fellow and research scientist at UC Berkeley in biochemistry and chemical biodynamics. She served on the board of directors of the Children's Hospital Research Institute in Oakland, California, and as a board member (the Chancellor's alternate) of BayBio, the regional voice of biotechnology in northern California. She was a former Executive Director of UC Berkeley's Office of Technology Licensing. Prior to her positions at UC Berkeley, Dr. Mimura was an analyst at Technology Forecasters, a consultant to Cor Therapeutics and Genomyx, and wrote for the *Genetic Engineering News*. Dr. Mimura's scholarly publications include articles on the sucrose phosphotransferase system in *Streptococcus mutans* and the histidine permease in *Salmonella typhimurium* in the *Journal of Biological Chemistry*; the *Proceedings of the National Academy of Sciences*; *Infection and Immunity*; *Analytical Biochemistry*; *Biochimica and Biophysica Acta*; the *Journal of Cellular Biochemistry*; *FEMS Microbiological Reviews*; *Advances*

in Enzymology; *Abstracts of the American Society for Microbiology*; and an article in the Fall 2006 *Journal of the Association of the University Technology Managers*, "Technology Licensing for the Benefit of the Developing World: UC Berkeley's Socially Responsible Licensing Program," Vol. XVII, No. 2, Fall 2006, which has been reprinted in *Industry and Higher Education* (Vol. 21, No. 4, August 2007).

Garry Neil, M.D., is Corporate Vice President, Corporate Office of Science and Technology (COSAT) at Johnson & Johnson World Headquarters in New Brunswick, New Jersey. In this role, Dr. Neil leads a team that catalyzes sustained growth for Johnson & Johnson by identifying and launching emerging technologies that underpin the creation of future businesses. Dr. Neil has broad experience in science, medicine, and pharmaceutical development. He has held a number of senior positions within Johnson & Johnson, most recently Group President, Johnson & Johnson Pharmaceutical Research and Development. Under his leadership a number of important new medicines for the treatment of cancer, anemia, infections, central nervous system and psychiatric disorders, pain, and genitourinary and gastrointestinal diseases, gained initial or new and/or expanded indication approvals.

Robert O'Neill, Ph.D., is currently Senior Statistical Advisor at CDER, FDA. Previously, he was for 20 years the Director of the Office of Biostatistics (OB) in the Office of Translational Sciences in CDER, which provides biostatistical and scientific computational leadership and support to all programs of CDER. Prior to October 1998, he was Director of the Office of Epidemiology and Biostatistics, responsible also for the postmarket safety surveillance of new drugs. From 1989 to 1990, Dr. O'Neill was a visiting professor at the Department of Research, University Medical School, Basel, Switzerland, where he developed and presented numerous lectures and created a course series for European pharmaceutical scientists, "Topics in Therapy Evaluation and Review (TITER)," which was the model for the European Course in Pharmaceutical Medicine (ECPM), a degree-granting graduate program. He is a fellow of the American Statistical Association (1985), a member of several professional societies, a past Member of the Board of Directors of the Society for Clinical Trials, the 2002 recipient of the Marvin Zelen Leadership Award in Statistical Science, and the 2004 Lowell Reed Lecture Awardee from the American Public Health Association.

Jason J. Paragas, Ph.D., serves as Associate Director for Science, Integrated Research Facility (IRF), Division of Clinical Research, National Institute of Allergy and Infectious Diseases (NIAID). He is also at DTRA as Special

Assistant to the Director, Dr. Alan Rudolph. He received his Ph.D. from Mount Sinai School of Medicine, New York University, studying the genetics requirements for influenza and vesicular stomatitis virus assembly. After his thesis work he was a National Research Council Fellow at the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID), where he later became a principle investigator. While at USAMRIID, Dr. Paragas developed cell-based antiviral discovery efforts in BSL-3 and -4 biocontainment, biotelemetry studies for nonhuman primates in BSL-3 and -4, and basic science investigations of Ebola and monkeypox virus pathogenesis. In response to the SARS outbreak, he identified a potential antiviral and developed a nonhuman primate model for the infection. He has also been involved in the DoD Cooperative Threat Reduction projects in the former Soviet Union, where he worked in Uzbekistan, Kazakhstan, Russia, and the Republic of Georgia. He led the development of the Threat Agent Detection and Response capability for the Republic of Georgia. This program was able to detect the first cases of avian influenza virus in the country. He was recruited by Dr. Jahrling to build a new group, Emerging Viral Pathogens section at NIAID. Since then he has been working as the Associate Director of Science, IRF, Division of Clinical Research, where he has responsibility for developing the scientific program, liaising between the builders and scientific program, and developing projects to support the IRF mission. Projects of particular note have involved developing medical imaging for infectious diseases, infectious disease systems biology, next-generation research informatics, and a novel risk management strategy for BSL-4.

Sudip Parikh, Ph.D., is Vice President of Health Policy at Battelle Memorial Institute and Managing Director of the Battelle Centers for Public Health Research and Evaluation. Dr. Parikh leads Battelle's engagement in health and life science policy and directs a diverse team of laboratory scientists; social, behavioral, and health services researchers; epidemiologists; statisticians; and survey and field data collection professionals. Prior to joining Battelle, Dr. Parikh served as Science Advisor and Professional Staff to the U.S. Senate Appropriations Committee, where he was responsible for negotiating the discretionary budgets of NIH, CDC, AHRQ, the Centers for Medicare & Medicaid Services, and BARDA. Dr. Parikh received his Ph.D. from the Scripps Research Institute in La Jolla, California, and his B.S. from the University of North Carolina at Chapel Hill.

Lili M. Portilla, M.P.A., has worked in the area of technology transfer at NIH since 1989. She has extensive experience in negotiating and developing commercialization strategies for complex, multiparty collaborations

and public–private partnerships. Ms. Portilla has broad knowledge of Federal and NIH technology transfer policy and law pertaining to biotechnology and commercialization issues. On December 23, 2011, Ms. Portilla was named Director of the Office of Strategic Alliances for the recently formed NCATS. From February to December 2011, Ms. Portilla served on a detail as Acting Director of the Technology Transfer and Partnerships at the NIH Center for Translational Therapeutics (NCTT), an intramural component of the National Human Genome Research Institute (NHGRI). NCTT is now the intramural program of NCATS. From January 2008 to 2011, Ms. Portilla served as Senior Advisor to the Director of the National Center for Research Resources (NCRR) and provided advice to NCRR staff on all facets of technology transfer, intellectual property, and public–private partnership issues. Prior to her position at NCRR, Ms. Portilla served for 7 years as Director of the National Heart, Lung, and Blood Institute (NHLBI), Office of Technology Transfer and Development (OTTAD). Ms. Portilla has also published several papers on public–private partnerships. She received a masters in public administration in 1992 from American University, Washington, DC, and a bachelor in business administration, double major in finance and Spanish literature in 1986 from Stephen F. Austin State University, Texas.

Jane Reese-Coulbourne, M.Ch.E., is the Executive Director of the Reagan-Udall Foundation for the FDA (Foundation). Created by Congress, the Foundation supports the mission of FDA by identifying, funding, and supporting public–private partnerships and projects that will provide the highest caliber science and technology to enhance the safety and effectiveness of FDA-regulated products. Ms. Reese-Coulbourne's background includes experience in patient advocacy, industry, and government. As an employee of the Procter & Gamble Company for more than 10 years, she worked in production operations, chemical engineering, government regulation, new technology, and product/brand start-ups. Later working with other Fortune 500 companies, she consulted in strategic planning, reengineering/restructuring, new technology plans and start-ups, and total quality management in unionized manufacturing and utility operations. Her diagnosis of breast cancer led to her interest in health research and patient advocacy, serving as Executive Vice President of the National Breast Cancer Coalition, and then as a consultant to the Director of NCI, as well as to leaders in not-for-profit advocacy organizations, foundations, and biotechnology/pharmaceutical companies. Ms. Reese-Coulbourne holds a B.S. in chemistry from the University of Mary Washington and an M.S. in chemical engineering from the University of Virginia.

Stephen Seiler, J.D., is a biotechnology entrepreneur and Founder of AesRx, LLC. Previously, Mr. Seiler had been Chief Executive Officer of several public and private biotech companies that he successfully led through restructurings and refinancing and/or trade sales. These companies include Idera Pharmaceuticals, Access Pharmaceuticals, and Effective Pharmaceuticals. Mr. Seiler was Executive Vice President, Planning, Investment and Development, at Elan Corporation plc from 1995 to 2001. He was part of a senior management team that transformed Elan from a small drug delivery company (1996 revenues, $200 million) into a fully integrated specialty pharmaceutical company (2000 revenues, $1.5 billion). From 1986 to 1995, Mr. Seiler worked as an investment banker in New York and London including founding and heading the Pharmaceutical Industry investment banking group for Paribas Capital Markets. Mr. Seiler is a member of the Board of Associates of the Whitehead Institute for Biomedical Research. He received a J.D. (honors) from Georgetown University, where he was an editor of the *Georgetown Law Review* and a B.A., summa cum laude, from the University of Notre Dame, where he was elected to Phi Beta Kappa.

Ellen V. Sigal, Ph.D., is Chairperson and Founder of Friends of Cancer Research (Friends), a cancer research think tank and advocacy organization based in Washington, DC. Friends is a leader in developing partnerships and advocating for policies that will get treatments and therapies to patients in the safest and quickest way possible. Friends works with federal health agencies, congressional leadership, academic research centers, and private-sector industry producing real results. Dr. Sigal is Vice Chair of the inaugural board of directors of the Reagan-Udall Foundation, a partnership designed to modernize medical product development, accelerate innovation, and enhance product safety in collaboration with FDA. She serves on the Board of FNIH, where she chairs its Public–Private Partnerships Committee. In 2010, Dr. Sigal was appointed to a 6-year term on the Board of Governors of PCORI as a representative of patients and health consumers. She also holds leadership positions with a broad range of cancer advocacy groups, public policy organizations, and academic health centers including the American Association for Cancer Research Foundation Board, Research!America Board, M.D. Anderson Cancer Center External Advisory Board, Duke University Cancer Center Board of Overseers, and The Sidney Kimmel Comprehensive Cancer Center Advisory Council.

Nancy Sung, Ph.D., is a Senior Program Officer with the Burroughs Wellcome Fund (BWF), having joined its staff in 1997. She oversees grantmaking of $13–$15 million annually in the areas of translational research and interfaces in science. This portfolio includes programs ranging from

individual bridging awards for postdoctoral fellows to midcareer awards for clinical investigators to institutional awards for interdisciplinary training programs that bridge the physical/mathematical and biological sciences. She has also shaped BWF's funding and activities in the area of clinical research policy and workforce development. Dr. Sung earned her undergraduate degree from the University of Pennsylvania and a Ph.D. in microbiology and immunology from the University of North Carolina at Chapel Hill. Prior to joining BWF's staff, Dr. Sung was a visiting fellow at the Chinese Academy of Preventive Medicine's Institute of Virology in Beijing, with the support of WHO and NIH-NCI. Dr. Sung is founding chair of the Health Research Alliance, a growing consortium of private foundations and voluntary health agencies with a shared interest in fostering basic science discoveries and removing barriers that prevent them from being translated into clinical studies and then into better health. She has served as a member of several IOM panels including the Clinical Research Roundtable. For 2011–2012, she is on sabbatical from BWF, serving in the National Science Foundation's Office of International Science and Engineering on its East Asia–Pacific portfolio.

Douglas C. Throckmorton, M.D., is Deputy Director for Regulatory Programs, CDER, FDA. In this role, he shares responsibility for overseeing the regulation of research, development, manufacture, and marketing of prescription, over-the-counter, and generic drugs in the United States. From aspirin to cancer treatments, CDER works to ensure that the benefits of approved drug products outweigh their known risks. Dr. Throckmorton is board-certified in internal medicine and nephrology, having received his training at the University of Nebraska Medical School, Case Western Reserve University, and Yale University. Prior to coming to FDA he practiced medicine at the Medical College of Georgia in Augusta.

Scott R. Ulrey, M.B.A., has been Deputy Director, Contracts Management Office, at DARPA since 2006 and held previous positions as division director and contracting officer at DARPA since 1989. He has more than 27 years of DoD acquisition experience, including tenure as head of the contracts section at the Special Programs Office, the White House Military Office, supporting White House classified acquisition programs. While at DARPA, Mr. Ulrey was the architect of the mechanics of Other Transactions issued pursuant to 10 U.S.C. § 2371 and personally trained the first military service and civilian representatives in developing their own Other Transactions. He is a recognized principal authority on Other Transactions and an expert in federal and DoD procurement contracts, grants, and cooperative agreements. Mr. Ulrey was also instrumental in the development of the first Other Transactions for Prototypes Program

Solicitation for the Tier II+ program, later known as the Global Hawk program, issued pursuant to 10 U.S.C. § 2371, and Section 845, the National Defense Authorization Act for FY 1994, and negotiated multiple systems programs such as the Orbital Express satellite servicing program. An active contributor to the success of acquisition reform initiatives and to the acceptance of innovative acquisition instruments in the acquisition community, he continues to provide advice, assistance, and training on Other Transactions directly to federal and DoD contracting activities. He received a B.A. in English and history from George Mason University and an M.B.A. from the Florida Institute of Technology. He is a Certified Professional Contracts Manager and has received numerous awards including the Office of the Secretary of Defense Exceptional Civilian Service Medal and Civilian Career Service Award.

William L. Warren, Ph.D., is a Vice President and heads the VaxDesign Campus of Sanofi Pasteur. The VaxDesign campus specializes in biomimetic systems such as an in vitro human immune system (MIMIC® System) to accurately assess new drugs and vaccines in a more predictive and physiologic way. Dr. Warren is a member of the Research and Development Management Committee, External Innovation Executive Committee, the New Vaccines Advancement Committee, and the Global Leader Network at Sanofi Pasteur. Prior to this, he was CEO and founder of VaxDesign Corporation before it was acquired by Sanofi Pasteur. He was also a Managing Partner of Sciperio Inc., which is an innovative high-technology development company. He directed a diverse portfolio of R&D programs as a program manager at DARPA in the Defense Sciences Office. Dr. Warren was a principal member of the technical staff at Sandia National Laboratories, and received his B.Sc. honors and Ph.D. degrees in engineering science from The Pennsylvania State University. He is a Fellow of the American Institute for Medical and Biological Engineering, has authored more than 190 referred publications, is the editor of 3 conference proceedings, has given more than 200 scientific presentations, and holds more than a dozen patents or patent applications. He has received three R&D 100 awards from non-volatile memories, to micro-dispensing systems, to a surrogate human immune system; the 2011 BioFlorida Company of the Year; the 2011 Florida Companies to Watch; the 2009 Outstanding Collaborator Award from DTRA; the 2009 Governor's New Product Award; the Schwartz Business Innovation Award; the Medical Marker Award; the Industry Week Innovation Award; the Discover Magazine Award; and several outstanding paper awards. He is on the board of directors and scientific advisory board of several companies and organizations, such as Florida's Blood Centers.

Lt. Col. Daniel J. Wattendorf, M.D., USAF, joined DARPA as a Program Manager in the Defense Sciences Office in 2010. His interests focus on applying methodological advances in genomics and biotechnology to optimize health and prevent disease—specifically to achieve simple solutions that improve health care at the point of care, anywhere. He holds a bachelor of science in microbiology from Cornell University and a medical degree with distinction from George Washington University. He completed a residency in family medicine at the National Capital Consortium; a residency in clinical genetics at the National Human Genome Research Institute (NHGRI), NIH; a fellowship in clinical cytogenetics at Georgetown University; and a fellowship in health policy from the Office of the Director, NHGRI, NIH. Lt. Col. Wattendorf previously served as Director, Air Force Medical Genetics Center and program manager for an Advanced Concept Technology Demonstration integrating advanced diagnostics and informatics with surveillance systems to rapidly detect natural and hostile pathogens in the Office of the Air Force Surgeon General. In addition to his DARPA programs, he is a geneticist at the National Naval Medical Center and the Cancer Genetics Branch, NCI, NIH.

Myrl Weinberg, FASAE, CAE, is President of the National Health Council (NHC), the only organization of its kind that brings together all segments of the health care community to provide a united voice for the more than 133 million people with chronic diseases and disabilities and their family caregivers. Made up of more than 100 national health-related organizations, the NHC's core membership includes approximately 50 of the nation's leading patient advocacy groups, which control its governance. Other members include professional and membership associations; nonprofit organizations with an interest in health; and major pharmaceutical, medical device, health insurance, and biotechnology companies. Ms. Weinberg's extensive career has focused on health care delivery, medical research, long-term care, and related issues that affect people with chronic conditions. She has testified repeatedly before Congress and federal regulatory bodies and is a frequent speaker on the patient perspective in health policy. Before joining the Council, she held numerous senior managerial positions at the American Diabetes Association, including Vice President for Corporate Relations and Public Affairs.

Michael Weingarten, M.A., is Director for SBIR Development Center at NCI, 1 of 27 Institutes of NIH in Bethesda, Maryland. In this role, Mr. Weingarten leads a team of nine Program Directors who manage all aspects of the NCI SBIR and STTR Programs, including a portfolio of over $115 million in grants and contracts annually. The SBIR and STTR Programs are NCI's engine of innovation for developing and commer-

cializing novel technologies and products to prevent, diagnose, and treat cancer. In his current role, Mr. Weingarten has implemented a set of key initiatives for optimizing the performance of the NCI SBIR Program at NIH. These include the establishment of a new model at NCI for managing the program—the SBIR Development Center. This Center is staffed with talented leaders from both industry and NIH who have expertise in the development and commercialization of technology in the cancer field to optimize the returns NCI achieves through this program. Under Mr. Weingarten's leadership, the NCI SBIR Development Center has launched a range of new programs to facilitate the success of small businesses in the cancer space. One of these new initiatives is a brand new funding program for the NIH known as the SBIR Phase II Bridge Award, which more than triples the amount of funding available to applicants through the NCI SBIR Program. The Phase II Bridge Award helps small businesses "bridge" the funding gap known as the "valley of death" that currently exists between the end of the SBIR Phase II Award and the next round of financing needed to advance a promising cancer therapy or imaging technology. This new award also incentivizes partnerships between NIH's SBIR Phase II awardees and third-party investors and/or strategic partners. Now in its fourth year, the NCI has made 12 Bridge Awards for a total of $31 million in NCI funding. These awards support projects in cancer imaging, molecular diagnostics, and drug development, including two projects that have advanced to Phase II clinical trials. Third-party investors, including venture capitalists and other strategic partners (e.g., big pharma), have provided more than $72 million in funding for these same projects. This provides NCI a leverage of more than 2 to 1 for every dollar it invests. For small businesses, raising funds from investors or strategic partners can still be a very difficult task. For this reason, NCI SBIR has launched an annual investor forum where potential investors can get a first look at the most promising NCI SBIR companies that are developing the next generation of cancer therapeutic, diagnostic, or imaging technologies. At the last forum in 2010, 6 out of the 14 presenting companies were successful in raising $225 million in private-sector funds. To put this into context, the amount of funds raised by NCI SBIR companies at the NCI Investor Forum was twice the value of the entire NCI SBIR budget. Prior to joining NIH, Mr. Weingarten was the manager of partnership development activities for NASA's Technology Transfer Program which included the SBIR Program. In his 12 years with NASA Headquarters in Washington, DC, Mr. Weingarten played a major role in the creation and design of NASA's Technology Transfer Program—a network of 10 NASA research centers and six regional technology transfer centers. Mr. Weingarten has a bachelor's degree in political science

from Northwestern University, Chicago, Illinois, and a master's degree in political science from Columbia University, New York, New York.

David Wholley, M.A., manages The Biomarkers Consortium for FNIH. He has also served as Director of the Genetic Association Information Network (GAIN), a public–private partnership dedicated to helping discover the genetic basis of common disease, and led the development of a major public–private partnership in drug safety with the biopharmaceutical industry and FDA. Prior to joining FNIH in 2006, Mr. Wholley's career spanned nearly 25 years in health care technology business management, including extensive experience in product development, sales, marketing, corporate strategy, and partnership and project development. Mr. Wholley has held senior management roles in several venture-funded technology start-up companies, including head of Global Marketing and Development for First Genetic Trust, Inc., which developed software for large-scale collaborative genetic research and personalized medicine. During a 16-year career at IBM, he co-led the corporate strategy team that guided IBM's formation of its Life Sciences industry organization and its first product, DiscoveryLink database integration software, in 2000. Mr. Wholley holds an M.A. from Rutgers University and a certificate in business administration from the Stern School of Business at New York University.

R. Sanders (Sandy) Williams, M.D., is President of the Gladstone Institutes, an independent, nonprofit research enterprise in San Francisco's Mission Bay. Gladstone is focused on finding solutions to some of the world's most relentless illnesses, including heart disease, neurodegenerative disorders, and life-threatening viruses such as HIV. Dr. Williams is a physician scientist who earned a bachelor's degree from Princeton University and an M.D. from Duke University. He completed a residency in internal medicine at the Massachusetts General Hospital; a cardiology fellowship at Duke; and conducted laboratory research at Duke, Oxford University, and the Cold Spring Harbor Laboratory. Prior to joining Gladstone in 2010, Dr. Williams directed cardiovascular medicine and research at the University of Texas Southwestern Medical Center, and then served as Dean of Medicine and Senior Vice Chancellor at Duke. In this latter role, he also was founding Dean of the Duke-NUS Graduate Medical School in Singapore. Dr. Williams is an elected Member of the IOM of the National Academy of Sciences, and is active at the interface of academia and industry in biomedicine. He currently serves as a Director on the boards of Bristol-Myers Squibb and the Laboratory Corporation of America.