National Institutes of Health
Turning Discovery Into Health

SCIENTIFIC MANAGEMENT REVIEW BOARD

MEETING SUMMARY – October 3, 2012

Board Members Present:

Norman R. Augustine, Chairman
Josephine P. Briggs, M.D.
William R. Brody, M.D., Ph.D.
Gail H. Cassell, Ph.D.
Anthony S. Fauci, M.D.
The Honorable Daniel S. Goldin
Eric D. Green, M.D., Ph.D.
Richard J. Hodes, M.D.
Stephen I. Katz, M.D., Ph.D.
Garry A. Neil, M.D.
Gilbert S. Omenn, M.D., Ph.D.
Roderic Pettigrew, M.D., Ph.D.
Susan B. Shurin, M.D.
Martha Somerman, D.D.S., Ph.D.
Clyde W. Yancy, M.D.

Ex-Officio Members Present:

Francis S. Collins, M.D., Ph.D.

Designated Federal Official:

Amy Patterson, M.D., Executive Secretary

Opening Remarks

Mr. Augustine welcomed Board members, panelists, and guests to the 13th meeting of the Scientific Management Review Board (SMRB). He briefly reviewed the meeting agenda and welcomed new SMRB member Dr. Martha Somerman and recently added members Dr. Garry Neil, Dr. Gilbert Omenn, and Dr. Clyde Yancy, who are serving on an *ad hoc* basis until their membership is finalized. Dr. Alan Guttmacher and Mr. Steven Burrill also have joined the SMRB but were unable to attend today's meeting. Dr. Eric Green and Dr. Susan Shurin will no longer serve on the Board; Mr. Augustine thanked them for their dedication, insight, and hard work as SMRB members. Former members of the SMRB may still serve the Board on an *ad hoc* basis. Brief member introductions were made.

Dr. Collins thanked the SMRB members for their efforts and expressed interest in the meeting agenda. He noted that, despite a challenging fiscal climate, exciting science is being performed, citing the recent publication of The Encyclopedia of DNA Elements (ENCODE) data, which included 36 peer-reviewed articles in numerous established scientific journals such as *Nature* and *Genome Research*. Dr. Collins acknowledged the uncertainty of the NIH budget as a result of the sequester that could be implemented in January 2013, which would result in an 8.2 percent retraction of the NIH budget, a loss of $2.5 billion. Dr. Collins informed the SMRB that he recently spoke at "Celebration of Science," a three-day event led

by *FasterCures* and the Milken Institute that involved more than 1,000 leaders from across the scientific research and policy communities. Dr. Collins thanked Mr. Augustine for his able leadership.

Mr. Augustine thanked Dr. Collins and reminded participants that there will be an opportunity for public statements during today's meeting and that written statements may be submitted to the SMRB at any time via smrb@mail.nih.gov. The minutes from the July 11, 2012, SMRB meeting were approved as written.

Dr. Patterson reviewed the NIH conflict of interest policy, and members reported no conflicts.

Dr. Patterson announced that Mr. Augustine will receive the American Patriot of Character award, which is a national award given annually to an American citizen whose leadership exemplifies the very best of our nation's founding principles and ideals. The award, given by the Character Education Partnership, will be presented in November 2012. Dr. Patterson read a quote from the president of the Research Corporation for Science Advancement about this announcement: "No one deserves this award more, as Norm Augustine has demonstrated true character, integrity and public commitment, in their value in achieving greatness, to his numerous and varied roles in national leadership. It's truly a rare person, and I would posit that a unique person, who combines the values and accomplishments that he represents as reflected in his business leadership, his government leadership, nonprofit leadership and his unparalleled championing of nation causes as an important American economic competitiveness. Norm Augustine is truly a man of character and he deserves all the recognition that he receives and he will no doubt continue to use that recognition to talk further with the American people about the challenge of maintaining our global economic competitiveness and the importance of science in that quest."

Overview of SMRB SBIR/STTR Working Group Process
Gail H. Cassell, Ph.D.
Member, SMRB SBIR/STTR Working Group

Dr. Solomon Snyder, chair of the SMRB NIH Small Business Innovation Research/Small Business Technology Transfer (SBIR/STTR) Working Group, was unable to attend today's meeting. Dr. Cassell took his place to lead a discussion about the progress of the Working Group. She reminded members that the impetus to consider SBIR/STTR programs at NIH includes the programs' size: $717 million is dedicated to the programs in 2012. Additionally, because NIH seeks fundamental knowledge about the nature and behavior of living systems, rather than focusing on developing products and technologies for NIH use, application of SBIR/STTR is a challenge. Identifying what has commercial value that aligns with the NIH mission can be challenging and complex.

Dr. Cassell briefly reviewed the reauthorization of the SBIR/STTR programs, which called for increasing the set-aside percentages for the next five years. Given this increase, it is important that NIH optimize its programs to operate at their fullest potential. Dr. Cassell also briefly reviewed the charge to the SMRB: "To recommend strategies for how NIH can optimize its utilization of the SBIR/STTR programs in keeping with the NIH mission." Dr. Cassell listed several considerations with respect to the SMRB charge: NIH should encourage the SBIR/STTR programs to foster innovation within small businesses that aligns with the priorities of the NIH Institutes and Centers (ICs), fund quality proposals yielding the greatest potential for successful commercialization, and leverage existing resources and expertise to enable the success of its grantees.

Dr. Cassell provided the roster for the SMRB SBIR/STTR Working Group:

Non-Federal	Federal
Solomon Snyder, M.D. *(Chair)*	Josephine Briggs, M.D.
William Brody, M.D., Ph.D.	Richard Hodes, M.D.
Gail Cassell, Ph.D.	Roderic Pettigrew, M.D., Ph.D.
Hon. Daniel Goldin	Susan Shurin, M.D. *(ad hoc)*
Arthur Rubenstein, M.B.B.Ch.	Harold Varmus, M.D.
Norman Augustine *(ad hoc)*	Michael Weingarten *(ad hoc)*

Dr. Cassell briefly reviewed the framework for deliberating organizational change and effectiveness as determined by a previous SMRB Working Group. She explained that the framework helps assess whether there is a need for change and how to optimize and implement change. She stressed that all endeavors should be transparent and efficiently communicated to stakeholders. Dr. Cassell also acknowledged previous reviews of the SBIR/STTR programs by NIH (2009), the National Research Council (NRC; 2009), and the Government Accountability Office (2006, 2011). She then turned to the life cycle for applications to SBIR/STTR grants, which ranges from the solicitation of applications to assessing research and commercialization outcomes of the program.

Dr. Cassell reviewed the preliminary findings, noting that the Working Group's impression of the SBIR/STTR programs ranged from "good to great." The Working Group believed that the programs have been quite useful and are meeting all statutory requirements. NIH currently allows ICs flexibility with respect to how they manage SBIR/STTR programs. Dr. Cassell stated that the programs vary in program management, size, budget, and, to some degree, success. Allowing such flexibility has both strengths and weaknesses, and this issue was the focus of the July 11, 2012, SMRB meeting.

Dr. Cassell briefly reviewed the 2009 NRC recommendations "designed to improve an already effective SBIR program at NIH," which included establishing reliable metrics and outcomes, strengthening the application process, enhancing scientific peer review, and defining and tracking success. She acknowledged that the establishment of metrics is important to assess the success of all discoveries and that commercialization provides its own challenges, particularly in light of the NIH mission to find causes and cures for disease.

Dr. Cassell ended her presentation by emphasizing the importance of the input from the panels assembled for today's meeting. These include representatives from the small business community, investors in biomedical innovation, and individuals who represent programs focused on improving a product's potential to be commercialized.

PANEL PRESENTATIONS

Panel Discussion I—Discussion with Representatives of the Small Business Community

Moderator

William R. Brody, M.D., Ph.D., *SMRB Member*

Panelists

Debra Ellies, Ph.D., *Founder, OsteoGeneX*
John A. Gardner, Ph.D., *Founder and President, ViewPlus Technologies, Inc.*
Paul Gross, *Chairman of the Board, Hydrocephalus Association (via teleconference)*
Rex Jakobovits, Ph.D., *President, Experiad, LLC (via teleconference)*

Anthony Ratcliffe, Ph.D., *President and CEO, Synthasome, Inc.*
Robert N. Schmidt, *Founder and Chairman, Orbital Research, Inc., and President, Cleveland Medical Devices, Inc.*
Steve Meginniss, *Co-founder, Magic Wheels Inc. (via teleconference)*

Dr. Brody thanked the panelists for attending today's meeting and briefly reviewed the goals for this session's discussion. The SMRB is soliciting input from cutting-edge innovators about their experiences in commercializing biomedical products and with the NIH SBIR/STTR programs, if applicable. Panelists were asked to consider ways in which these programs could be strengthened, taking into consideration each step of the SBIR/STTR life cycle. In addition, panelists were asked to discuss the role of SBIR/STTR programs in the commercialization process and to consider metrics for evaluating grantees' success.

The panelists spoke in turn on their relevant experience.

Debra Ellies, Ph.D.
Founder, OsteoGeneX

Dr. Ellies introduced herself as the founder of the company OsteoGeneX, which received SBIR phase I and phase II grants in addition to other grant awards. In total, OsteoGeneX has received $5 million in grant awards and angel investment. She emphasized that government funding has been crucial for her company.

Dr. Ellies noted that she also has been a reviewer for SBIR grants. She stated her belief that many applicants need to place more emphasis on validating the value proposition of their end product in order to understand the market being pursued. She also recommended the inclusion of industry experts as reviewers to place more emphasis on the commercial aspects of grant applications.

Dr. Ellies explained that her company uses high-throughput screening to identify factors to assist in building bone for treatment of osteoporosis; it specifically focuses on sclerostin and Wnt modulators. The company is currently developing a series of antibodies, some of which are in phase II or III trials for optimization.

Dr. Cassell asked Dr. Ellies whether advice on preparing a product for commercialization was easily accessible and whether a scientific advisory board provides such input. Dr. Ellies replied that OsteoGeneX is fortunate to have a medicinal chemist on staff and noted that generally the company seeks advice from people with both experience in industry and experience preparing a drug for the market.

Dr. Katz commented that sclerostin is a popular target, making the current market quite competitive. Dr. Ellies replied that she was the primary inventor and discovered sclerostin's mechanism of action and the first series of blocking antibodies. She explained that she is aware of most of the competition in the field and that interactions are important in order to avoid redundancy.

Dr. Omenn asked Dr. Ellies what she believed were reasonable metrics for assessing an invention's progress. She acknowledged that it is a difficult question, particularly when most companies will license a technology rather than develop it themselves. A licensed product would be farther along

than any of the technologies currently being developed at OsteoGeneX. Dr. Ellies stated that milestones could include partnering with another company, receiving matching equity, and stages related to clinical trials and the status of an Investigational New Drug (IND) application. Applying metrics to preclinical development would be challenging.

John A. Gardner, Ph.D.
Founder and President, ViewPlus Technologies, Inc.

Dr. Gardner informed the SMRB that he is a trained material physicist who woke up blind one day in September 1988. At the time, he was running a successful academic laboratory with a number of graduate students, and although he was able to use the assistance of his students and colleagues, he was unable to read and interpret the data from his own laboratory. As a result, he began working on ways to improve accessibility to complex information graphics and developing new technologies. The first product from his company became available in 2000, funded through money from Dr. Gardner and his friends. The company was able to break even in 2003 with the addition of SBIR funding, which also allowed it to sustain a large research and development division. Now, ViewPlus Technologies, Inc., is a multimillion-dollar company with several hundred employees.

Dr. Gardner informed the SMRB that he received SBIR funding from three government agencies. He expressed the opinion that NIH's method for managing SBIR grants was preferable, although he noted that he was not able to comment on broad policy issues. He stated that establishing indirect cost rates for SBIR funding is extremely challenging and expensive. Another challenge is that the limits required in the SBIR audits have not adjusted for the rate of inflation.

Dr. Gardner informed the SMRB that every SBIR-funded project at ViewPlus Technologies, Inc., has resulted in a product and that the majority of products were able to reach the marketplace near the end of a phase II grant. ViewPlus Technologies, Inc., is now established and does not require grant funding for sustainability.

Dr. Gardner stated that NIH's scientific review process for SBIR grants is appropriate; panel members are generally aware of the criteria required for an SBIR grant, which are different than those for an academic research proposal. He acknowledged that one panelist can significantly influence funding decisions in review panels, which is appropriate when that person thoroughly understands the application and the process. He supported including industrial expertise on review panels; in his experience, many review panels included people with medical degrees who had little experience with SBIR.

In response to questions, Dr. Gardner added that he has received between six and eight SBIR grants from NIH, all from the National Eye Institute.

Paul Gross
Chairman of the Board, Hydrocephalus Association

Mr. Gross joined the meeting via Skype. He stated that he is an entrepreneur and an executive in the software business. He also is the father of a child with hydrocephalus. He noted that his son is treated with a medical device called a shunt that has a very high failure rate; approximately 50 percent fail within two years. Mr. Gross chose to focus on the most common point of failure and attempt to solve the problem. He found a laboratory at the University of Utah with a similar

interest, as well as an individual with 23 patents on shunt design and similar intellectual property. Together, they tested the feasibility of their shared concept.

Initially, Mr. Gross and his colleagues were able to secure philanthropic funding with the intention of establishing their research to the point of securing a SBIR award. The work began as a collaboration in which a director of engineering oversaw production, the lab director managed the employees actively testing the product, and Mr. Gross worked on the application infrastructure on grants.gov and drove the process. Mr. Gross stated that his research group believed an SBIR grant was more appropriate than an STTR grant simply because it was more financially beneficial. He personally found the application process complicated and said that communication with the program manager was sometimes unclear. He also found it extremely challenging to balance the objectives of the university, which sought to publish findings and advance careers, with the commercial desire to protect intellectual property and move quickly.

Mr. Gross reported that his research group was not awarded the SBIR grant. Because the group had submitted an application in response to an announcement funded by the American Recovery and Reinvestment Act, resubmission was not possible. He said he still has a strong desire to see device innovations come to market and to have a small team that can provide access to capital, engineering, and marketing experience. Mr. Gross and his colleagues researched previously funded SBIR grants to determine what might make their application more competitive and found the funded grants to cover a wide, inconsistent range of projects. Some appeared too academic or lacked market awareness. Companies with strong engineering experience attempting to tap into the marketplace appeared to lack clinical expertise or access to patients.

Rex Jakobovits, Ph.D.
President, Experiad, LLC

Dr. Jakobovits informed the SMRB via teleconference that he acquired his Ph.D. in computer science in the late 1990s and discovered the SBIR program through a National Institute of Mental Health official who approached him after hearing him present his work at a human brain conference. He believed it was likely that he would have gone into industry had he not heard about the SBIR program. Dr. Jakobovits explained that he went on to receive phase II and fast-track SBIR funding totaling $2 million. The investment went toward a medical imaging software program for hospitals, which provided a platform for sharing imaging data. At the time of the fast-track funding, the company was able to generate revenue, and approximately one year later, the company was earning $1 million in profit and was acquired by McKesson Corporation. Dr. Jakobovits noted that a niche for this product had to be created and that SBIR funding was the only way he could obtain the resources to create the product. He explained that in addition to being profitable, his product is an example of successful software implementation and now has 60,000 to 70,000 registered users.

Dr. Jakobovits suggested that the SBIR program should be adjusted to prioritize funding for new investigators or have a monetary cap on the amount of funds provided over a specific time frame. He believed that making allowances for new investigators could have a significant impact on commercialization outcomes for SBIR awardees. He added that, while serving as a reviewer, he noticed that some companies have apparently found a formula for securing good funding scores.

Dr. Jakobovits emphasized the need to shorten the time from grant submission to award because it is difficult for new companies to wait for funds, particularly when a grant application must be resubmitted.

Dr. Jakobovits observed that reviewers do not consistently weigh the importance of commercialization potential as part of the funding decision and suggested that aspects of the review process be standardized. He said that reviewers should ask, "Can this result in a product or a service that will generate more revenue or create jobs beyond some multiple of the money that is being spent?" He gave an example of a review panel for behavioral technologies, wherein many of the submitted proposals were for building multimedia training material for a specific disease. None of the proposals had a commercial potential beyond perhaps $100,000 in revenue. Many reviewers were giving these proposals good scores because they believed in the need for training, but Dr. Jakobovits argued that greater scrutiny for commercial potential is warranted.

Anthony Ratcliffe, Ph.D.
President and CEO, Synthasome, Inc.

Dr. Ratcliffe introduced himself as someone with an academic background who went into private industry and now runs a biotechnology company in San Diego. He complimented the SBIR program, particularly at NIH, for providing an invaluable service and cautioned that any changes made should be carefully considered. He acknowledged that there is opportunity for improvement but stressed the importance of the SBIR program.

Dr. Ratcliffe interpreted the role of the SBIR program as enhancing the commercialization pathway at the earliest stage, when a product is high risk but shows the potential for high reward. Worthwhile products generally receive further investment by private industry. He stated that although this system tends to work well, the current economic climate has caused a major disconnect between the end of SBIR funding and investment from the private sector. Dr. Ratcliffe stressed that this problem must be addressed. He suggested a SBIR funding opportunity similar to the academic R21 funding mechanism, wherein high-risk innovative products could receive funding to improve their odds of success. He also suggested ways to improve commercialization: (1) improve the commercial feasibility assessment during the review process to ensure that the financial aspects of the grants are as strong as the scientific aspects; (2) consider a more formal phase III funding process to include initial clinical trials; (3) inform the private sector about the potential of new products by giving entrepreneurs and venture capitalists opportunities to meet; and (4) consider public-private partnerships as a mechanism to bring venture capital to SBIR participants.

Dr. Ratcliffe reiterated the need for transparency in the review process and quick funding decisions for small businesses. He also suggested that NIH consider allocating a small percentage of SBIR funds toward patent expenses. Lastly, he suggested that introduction of a product to a patient could be a valuable metric.

In response to questioning, Dr. Ratcliffe clarified that Synthasome, Inc., focuses on products involved in soft tissue repair for orthopedics. The company has received four to six SBIR grants and has no venture capital investment.

Robert N. Schmidt
Founder and Chairman, Orbital Research, Inc., and President, Cleveland Medical Devices, Inc.

Mr. Schmidt introduced himself as an entrepreneur with a background in engineering; he has been involved in the creation of five companies that make medical devices and employ a total of 70 people. His companies have received dozens of SBIR grants and several major awards, including an Edison Award in 2012. Mr. Schmidt briefly reviewed some of the products created in his companies, noting that cost savings from improved devices can also be considered a return on SBIR investment.

Mr. Schmidt stressed that NIH should promote the marketing of inventions as quickly as possible. This will allow job creation and, by extension, wealth creation. Investing in these technologies is critical, and securing patents is a priority for protecting intellectual property. He encouraged NIH coordination with other government agencies.

Mr. Schmidt expressed the opinion that the "tank of basic research is overflowing" and that too many potential technologies are neglected because of the sheer volume of basic research. He equated SBIR with a valve to this tank: Funneling more money to SBIR would allow the technologies in the tank to flow on toward commercialization.

Mr. Schmidt noted that in 2005, 38 percent of small businesses were run by engineers and scientists compared to 8 percent in 1975. This number may now be larger. Small businesses receive only 4.3 percent of the research and development funding, yet they produce 10 times the wealth created by large businesses and universities. Mr. Schmidt added that small businesses are the most effective at growing new jobs; from 1989 to 2005, they created 93 percent of reported new jobs.

Mr. Schmidt argued that funding for technology transfer, including patent costs, should be increased. He said it was his understanding that NIH is the only government agency that does not allow the use of SBIR funds toward patent costs.

Mr. Schmidt recommended that interagency committees, specifically including the U.S. Food and Drug Administration (FDA), be created to speed approval for the market. Other agencies with which NIH could collaborate include the Department of Defense, the Department of Veterans Affairs, and the Centers for Medicare & Medicaid Services.

Mr. Schmidt noted that there are five major metropolitan areas in the U.S. where venture capital is invested for biotechnology. He cautioned that encouraging the link of venture capital funds with commercialization will result in a reduction in geographical diversity.

Lastly, Mr. Schmidt mentioned the negative effect of the the Leahy-Smith America Invents Act.

Steve Meginniss
Co-founder, Magic Wheels, Inc. (via teleconference)

Mr. Meginniss explained that his first company, Sonicare, was created with SBIR funding in 1990 and grew to have more than 500 employees and several million dollars in sales. Once Sonicare was established, Mr. Meginniss opted to look for other technology to which he could apply the same business model. He found that, in 1990, the National Institute of Disability Rehabilitation Research in the Justice Department had performed a polling project on mobility and determined the need for multiple gears on wheelchairs. Mr. Meginniss worked to redevelop a two-gear wheel licensed by the University of Washington and sought SBIR funding. The grant was rejected in the first round; in the

second round, the 3-D graphics and animation used in the proposal were so convincing that reviewers believed that the product had already been built. The proposal was again rejected, but toward the end of the 1998 fiscal year, Mr. Meginniss was informed that he would be receiving surplus funds. Mr. Meginniss worked on the project in his basement. Once he had proven the concept, he was awarded phase II SBIR funding to refine the product, and a phase II continuation grant allowed him to get the product ready for production.

Mr. Meginniss explained that he found complexity in the market that he had anticipated—the product had to be priced at almost triple the actual cost to get insurance coverage. He found that the rehabilitation industry requires an enormous cost markup, and a product can face pricing problems when the volume is low and the cost is too high. Magic Wheels, Inc., has received $5 million is angel funding, but it has never broken even. Mr. Meginniss expressed surprise that the company is still in existence after 16 years. He stated that SBIR funding gave Magic Wheels an opportunity, but it is up to the inventor to follow it through. He acknowledged that support for commercialization would be helpful but noted that the rehabilitation market is unique.

Discussion

Mr. Augustine thanked the panelists for their contributions. He acknowledged that the time frame for grant support does not accommodate the needs of small businesses, and the "valley of death" exists primarily because of the amount of funds required to drive a product to commercialization. Mr. Augustine noted that there are inherent conflicts between the stakeholders in these businesses. For example, university researchers must "publish or perish" whereas in private industry, one might "publish and perish." The fiscal cycles also differ. In addition, the government tends to be risk-averse whereas businesses are not. Given these conflicts, he asked the panel what they might suggest to the SMRB. Dr. Ratcliffe responded that the goals of the different parties need not be the same, but they need to be aligned. This is true of many partnerships.

Mr. Schmidt stated that entrepreneurs are, by nature, risk takers and stressed the need for more funding, perhaps in the form of phase IIb or phase III funding mechanisms. He also urged funding support for patenting technologies. Dr. Matthew Portnoy, manager of the NIH SBIR/STTR programs, clarified that NIH, the Department of Homeland Security, the National Aeronautics and Space Administration, and the Department of Agriculture do not allow SBIR funds to be used for patent costs; the Department of Defense may allow it depending on specific agency regulations, and companies can negotiate the costs as part of the indirect cost rate. SBIR awards can include a 7 percent "fee" and companies are not restricted in how they use that fee and could apply it to patent costs. However, NIH does not allow patent costs to be reimbursed on their direct awards.

Mr. Meginniss noted that an initial patent filing is inexpensive, whereas prosecuting a patent is very expensive. Mr. Schmidt agreed but noted that the U.S. Patent Office can take seven to eight years to issue a patent. With the current process, larger companies can overpower small companies by flagging patents and delaying their progress. He estimated that it costs between $2.5 and $5 million to obtain a patent. Dr. Ratcliffe agreed, urging NIH to allow grantees to apply a small amount of direct costs to patent costs. Mr. Meginniss agreed that patent prosecution is extremely expensive but did not consider using grant funding to pay for it appropriate.

Dr. Omenn asked whether the increased funds from the set-aside in the reauthorization could be applied to aspects of commercialization beyond phase II. Dr. Portnoy explained that the SBIR/STTR

programs are forbidden from funding phase III awards; however, there are provisions that allow creativity. For instance, NIH is currently establishing a commercial readiness pilot as a follow-up award.

Dr. Ellies noted that grant reviewers tend to be tasked to prioritize innovation, but the path to commercialization is largely uniform.

Dr. Brody summarized the discussion. NIH SBIR applications encompass a broad range of technologies, which exemplifies the need for flexibility in how funding is managed. He recognized that the grant review cycle should be shortened and that the review process should include more focus on commercialization potential. SBIR mills are still a concern, although new reporting requirements in the SBIR reauthorization may help to address this issue. Some of the funding rules for SBIR are considered problematic, although creativity can be applied to the funding mechanisms to assist inventors. Patent costs should be considered. Some consideration should be given to how to best address the "valley of death." Dr. Cassell added that the speed of the FDA approval process should also be considered; including FDA earlier in the process may aid inventors by allowing them to address FDA requirements as they develop the technology.

Public Comments

There were no public comments.

Panel Discussion II—Discussion with Investors in Biomedical Research
Moderator
Hon. Daniel S. Goldin, *SMRB Member*
Panelists
Kristina Burow, M.B.A., *Managing Director, ARCH Venture Partners*
Alex de Winter, *Partner, Mohr Davidow Ventures*
Allan W. May, *Founder and Chairman, Life Science Angels, Inc.*
Andrew J. Schwab*, Managing Partner, 5AM Ventures*
Armen Shanafelt, Ph.D., *Venture Partner, Lilly Ventures*

Hon. Goldin opened the session by explaining that it is important to gain the perspective of private investors who will help SBIR grantees finalize their products for market. He briefly reviewed the data collection process for the SBIR/STTR life cycle. The goals of this session are to solicit input from entrepreneurs regarding their experiences investing in biomedical products developed by small businesses; to describe the characteristics of projects that successfully commercialize products and identify associated milestones for predicting their success; and to discuss the role of SBIR/STTR programs in the commercialization process and identify ways in which these programs could be strengthened. Hon. Goldin also requested that the panelists comment on whether investors should be part of the SBIR/STTR review process and how to deal with potential conflicts of interest.

Kristina Burow, M.B.A.
Managing Director, ARCH Venture Partners

Ms. Burow explained that ARCH Venture Partners is a 26-year-old technology transfer fund company that started through the University of Chicago and invests in more than 150 companies, including many academic and national laboratories. She explained that the company tends to be the first to

invest in the technologies that it chooses because ARCH historically focuses on high-risk, "holy grail" science. Currently, $1.5 billion is under management at the firm. Ms. Burow provided an example of research that ARCH supported: a company called Ikaria, which induced suspended animation in mammals using hydrogen sulfide to put mammals into a state similar to hibernation. ARCH seeks inventors who perform one or two key experiments that will fundamentally de-risk a technology. No technology can be completely risk free, and not all investments result in a new innovation, but ARCH seeks out investigators performing innovative research who have addressed some of the fundamental aspects of success. Ms. Burow provided another example of the type of company in which ARCH invests: Siluria is a company that economically converts methane to ethane. She noted that larger companies have sought to create this technology for years to convert natural gas, a highly abundant resource, to liquid fuel. Siluria seeks to convert methane to in-demand chemicals, plastics, and fuels.

Ms. Burow acknowledged that NIH has supported great research and improves the lives of billions of people. She expressed the belief that NIH is a tremendous asset to the U.S. because government support is necessary to promote basic research. Ms. Burow stated that mainstream investors are not comfortable with high-risk technologies, but if the impact is large enough and the risk is addressable, such research should be supported. She commented that U.S. investment in this type of technology is critical to keeping this country competitive. She noted that the U.S. recently successfully landed the rover *Curiosity* on Mars and stated that these types of ambitious endeavors must continue.

Hon. Goldin added that *Curiosity* was born out of a failed Mars mission in 1998. He noted that the human brain learns by making errors and that within a few months after the failure, the concept for *Curiosity* was conceived. He quoted Winston Churchill, who said, "Success is nothing more than going from failure to failure with undiminished enthusiasm."

Alex de Winter, Ph.D.
Partner, Mohr Davidow Ventures

Dr. de Winter informed the SMRB that his background is in the life sciences. He has worked for several start-up companies, including one company involved in the Human Genome Project. He acknowledged the importance of government funding to promote scientific innovation. Dr. de Winter also has served as a scientific reviewer for the SBIR program at the National Cancer Institute (NCI) for phase IIb funding applications, so he has had the opportunity to see both sides of the SBIR funding process. He noted that very little attention is paid to patents or patent costs.

Dr. de Winter explained that as a venture capitalist of phase IIb technologies, he places emphasis on the efficiency and efficacy of the management team. Bringing a new technology to market typically involves challenges beyond scientific challenges, and the ability to overcome them is primarily determined by the ability of the leadership team.

Dr. de Winter also estimated that the maximum SBIR funding for phase I to be close to $250,000, whereas for phase II it is $500,000. Although this amount is good seed funding, it remains to be a small amount—sometimes only a month's worth of expenditures—and the money is not always worth the effort to obtain it. Dr. de Winter praised NCI's efforts to foster communication between private investors and entrepreneurs through investor forums. He also acknowledged that companies

that have received SBIR funding are generally considered well vetted; such companies are likely to be taken seriously by private investors.

Allan W. May
Founder and Chairman, Life Science Angels, Inc.

Mr. May introduced himself and stated that, although he is a venture capitalist, he wanted to discuss angel investing. He founded a company called Life Science Angels and is chair of the Angel Resource Institute (ARI, http://www.angelresourceinstitute.org/research). As noted on ARI's Web site, "One of ARI's main goals is to gather robust data on angel groups, so that the foundation and academic research community can analyze the data and produce research that informs policy makers, entrepreneurs, investors and academia." ARI promotes and teaches about angel investing. Mr. May stated that it is important for NIH to understand the investment landscape. Due to the recent economic challenges, investment of venture capital in health-related projects has declined significantly; approximately two-thirds of funds that were available prior to the downturn are no longer available. He believed that not only does NIH need to be more effective, but SBIR funding for health sciences now serves a more critical role.

Mr. May informed the SMRB that a new funding model is currently being formed, but there is a great deal of fluctuation. Currently, angel investing places $20 to $22 billion per year into the U.S. economy—the same amount as venture capital. Mr. May stressed that angel investing, unlike venture capital, uses personal funds to support technology. Another difference is that virtually all angel money is seed money, whereas venture capitalists tend to invest at a later stage of the process. Angel investing is an important part of the funding process that should be considered a potential next step for SBIR-funded small businesses.

Mr. May explained that three aspects of small business health technology should be considered: money, mentoring, and data. Currently, 85 percent of investment in medical technology goes offshore. Also, valuations have not increased. The "valley of death" means that significant data, such as clinical trial data, are needed to procure additional funding. Mr. May noted that the financing climate is tight, and funding in early start-up (A series) or later expansion of operations (C series) round of investment is essentially the same, leaving no motivation to invest early. Changes in valuations must take place to encourage earlier investment. Mr. May estimated that approximately $2 to $3 million is required to ready a medical device for market, whereas $3 to $5 million is required for drug development.

Mr. May recommended that local angel groups be included in the SBIR application review process or as mentors. It has been estimated that proper mentoring of entrepreneurs is worth anywhere $500,000 and $1 million. Angel mentors are typically entrepreneurs who have cashed out on their inventions and understand the commercialization pathway. Entrepreneurs' ability to show they have access to this type of direction is important for procuring funding. Mr. May suggested that funding for later stage SBIR grants could require angel investment for commercial validation. Lastly, viable data to understand the contribution of angel investment are lacking. ARI is currently drafting the "Halo Report" to better understand the current climate of angel investing. Mr. May expressed the belief that this type of data collection through nonprofit organizations like ARI should be supported by NIH.

Andrew J. Schwab

Managing Partner, 5AM Ventures

Mr. Schwab informed the SMRB that 5AM Ventures is located in California and Massachusetts and focuses on drug discovery technologies. Similar to ARCH Venture Partners, the company seeks out investments in big ideas in the early stages of technology development. Funded companies are typically in the preclinical stage with an established proof of concept. Ensuring that the companies have sufficient funds to assist their technologies through the development process is critical. Currently, ARCH operates on a $220 million fund.

Mr. Schwab acknowledged that SBIR/STTR funding does not affect his company because it invests early in the technology process. Of 5AM Ventures' approximately 40 investments, only one or two have SBIR/STTR funding. He noted that successful, repeat entrepreneurs typically do not require government funding to obtain capital because they have other resources. He also stated that many find that the waiting period to receive SBIR funding is not worth the effort required to obtain it. He agreed with the previous panelist that alignment of goals among the stakeholders would be advantageous. Important goals to consider include job creation and getting products to patients.

Mr. Schwab expressed the belief that venture capital or other outside funding is necessary to get a new drug ready for market. He stated that many venture capitalists would be happy to serve as mentors to entrepreneurs.

When asked about 5AM Ventures' involvement in peer review of SBIR grants and potential conflicts of interest, Mr. Schwab stated that the number of companies in which 5AM invests is small compared to the overall pool of research projects it considers. In the event that a technology of interest to 5AM does cause a conflict, there should be a process to ensure that the venture capital reviewer does not make critical funding decisions. In general, he believed that reviewer input from a venture capitalist would strength the SBIR/STTR review process.

Armen Shanafelt, Ph.D.
Venture Partner, Lilly Ventures

Dr. Shanafelt acknowledged that he had very little experience with SBIR funding and therefore may have a different perspective. Lilly Ventures started as part of Eli Lilly and Company and became a separate entity in 2001. It remains a traditional venture capital firm with the distinction that it has one source of capital (Eli Lilly and Company). Dr. Shanafelt stated that the involvement of a limited partner with an understanding of the life sciences is very important. Lilly Ventures has approximately $175 million in capital and funds technologies at a variety of stages of development. Lilly Ventures prefers to invest in platform companies focused on creating molecules with the potential for major impact.

Dr. Shanafelt acknowledged that a significant part of science is failure. However, it is critical to think that the endeavor will be useful if it is successful. An important question to consider is: How do you determine what technology is likely to succeed? With therapeutics, there can be a significant time interval between discovery and product; some of the current drugs on the market were predicted 10 to 12 years ago. The time of investment may be shorter, but the commercialization plan must be in place.

Dr. Shanafelt expressed the belief that the valley of death is caused in part because we know very little about human disease. A drug's efficacy cannot truly be assessed until the drug can be tested in human clinical trials. Investors cannot base their decisions about a technology in its early development on an assumption of efficacy; therefore, they must also consider the technology's utility. They must consider whether a technology is differentiated enough from current technologies to be worthy of investment. Dr. Shanafelt added that critical milestones should be defined to assess success.

In Dr. Shanafelt's estimation, the funding amounts and time frames for SBIR awards should be reconsidered. He questioned whether SBIR funding for commercialization was the correct goal. He preferred the use of SBIR awards as seed funding for critical experiments.

Discussion

Dr. Katz asked the panelists how they assess whether a technology is likely to make an impact. Dr. Shanafelt replied that both individuals within Lilly Ventures and outside consultants help the company make assessments. Because of its ties with Eli Lilly and Company, Lilly Ventures has access to partnerships and ties to leverage its knowledge and acquire information. Investors must use critical thinking to assess the current market to determine whether the current technology is sufficient and whether the new technology is realistic.

The group briefly discussed rheumatoid arthritis (RA) inhibitors as an example. Dr. Katz noted that there are new models to approach RA, but lag time between concept and product is significant, making it difficult to predict whether the technology will be sufficiently differentiated from other products in the marketplace. One must have a vision of the future, Dr. Shanafelt acknowledged, while being limited by what is known today. It is entirely likely that other people will have a similar idea. Even with differentiation of their strategy or approach, inventors can encounter unexpected competition. He noted that, in the case of RA inhibitors, a number of drugs are doing well, so sometimes there is room in the marketplace. It can be possible to find a niche. Mr. May offered that investors typically do not lose money on the science or technology, but rather to the commercialization process or lack of a proper team to lead the project. Choosing the correct people and commercialization pathway is critical.

Dr. Pettigrew noted that the panelists seemed to differ on whether human data are needed to acquire venture capital funding; Mr. May said they were required whereas Dr. de Winter and Mr. Schwab said they were not necessary. Ms. Burow explained that most of the technology in which ARCH invests does not have human data but that those that do tend to acquire attractive deals with pharmaceutical companies. For example, Lycera partnered with Merck to create an anti-tumor necrosis factor molecule for RA; it was an unusual target and therefore of interest to Merck. Another example is Agios, which made a $140 million cash deal with Celgene for a preclinical technology platform. She explained that there are cases in which phase I and IIa data may be necessary, but if the market and idea are good enough, even larger companies will invest in a technology. Mr. Schwab added that the number of investors willing to invest in preclinical technologies has dipped precipitously, to perhaps 20 percent of the number of willing investors pre-2008. Mr. May agreed, noting that scale is a concern. He estimated that angel investing is approximately one-third of its total before the economic downturn.

Dr. Omenn reiterated that the valuation of technologies is similar in the early versus later stages of development and asked how people can be encouraged to invest in those circumstances. Ms. Burow replied that ARCH Venture Partners typically will not fund Series C (later phase) technologies but will work with corporate partners at that stage. She remarked that for the last several years, "Down is the new flat, and flat is the new up" in terms of annual budgets. She encourages inventors to start considering corporate partnerships in the early stages of development. Mr. May referred to the initial purchase offer of Genex Cooperative, Inc., noting that the money raised in the initial purchase offer did not cover the company's original investment. The risk of investing early can and does dissuade investors. Mr. Schwab added that that is why the right team is critical.

In response to questioning, Mr. May explained that the National Venture Capital Association marshaled the Medical Innovation and Competitiveness Coalition (MedIC) to emphasize America's medical innovation. MedIC has released a report showing the decline in life science investing and indicating that venture capitalists are less likely to invest in early-stage technology. Of those companies funded, 85 percent or 86 percent go offshore to perform clinical work, and an increasing number stay offshore and do not file for pre-market approval through the FDA.

Dr. Cassell remarked that Russia has a program similar to SBIR. That program's challenge was not access to funds, but rather the ability to identify projects worthy of funding. Participants in a recent forum on U.S. and Russian biomedical sciences concluded that money is not spent in Russia due to the lack of intellectual protection and infrastructure. Dr. Cassell suggested that funds be matched for research in Russia without losing intellectual property. Dr. de Winter replied that it is difficult to convince investors to consider that type of investment, although they may do so independently of venture capital firms. He noted that co-investment is already taking place. Mr. May added that they have invested in biomedical technologies that considered moving to Russia but that the offer for support for the relocation and research costs was not considered sufficient.

Hon. Goldin thanked the panel members for their input.

Dr. Collins showed the SMRB a brief video from a recent conference titled "Celebration of Science," which was held in Washington, D.C., and on the NIH campus, September 7–9, 2012. This event was sponsored by *FasterCures* and the Milken Institute to reaffirm America's commitment to bioscience. SMRB members thanked Dr. Collins for showing them the video, and Mr. Augustine noted that the video contains provocative testimony that could be used to demonstrate to Congress the importance of biomedical research in the U.S. The video can be found at http://youtu.be/4Q4SQGUug8o.

Public Comments

There were no public comments.

National Advisory Council on Innovation and Entrepreneurship
Gururaj "Desh" Deshpande, Ph.D.
Co-chair, National Advisory Council on Innovation and Entrepreneurship

Dr. Deshpande introduced himself and informed the SMRB that he has founded a number of companies throughout his career. He has been asked to comment on the National Advisory Council on Innovation and Entrepreneurship (NACIE), part of the Department of Commerce, and the

Deshpande Center for Technological Innovation at MIT. He explained that 500,000 new companies are formed in the U.S. each year, generating 4 million jobs.

Dr. Deshpande stated that the four criteria needed to speed company formation are: (1) a good idea, (2) entrepreneurs, (3) mentors, and (4) access to capital. NACIE has contributed to both the Startup America Initiative and the Jumpstart Our Business Startups (JOBS) Act. He explained that, 12 years ago, big ideas came from the funding of private companies such as Bell Labs and IBM. That type of funding no longer exists. We must now ask, "How do we make research ideas have a bigger impact?" because there is a global economy and because companies are less likely to generate ideas. At MIT, he wanted to find ways for the university to be a source of ideas for entrepreneurs. Dr. Deshpande explained that ideas must be relevant to be effective; in other words, innovation plus relevance equals impact. He stated that the Nobel laureates asking profound questions should be left to their work, but other people have important ideas that add value to society as well, and these ideas should be fostered. Innovation cannot be mandated, and in the university setting it is possible to lose sight of the importance of impactful knowledge. The best innovators tend to patent their inventions and then market their products.

At MIT, Dr. Deshpande attempted to connect faculty and graduate students to the concept of relevance at the outset. He stressed that the best way to promote innovation for the marketplace is to select, connect, and direct. Researchers with an idea are given a small grant, between $50,000 and $100,000, and are mentored by "catalysts"—venture capitalists who volunteer to mentor grantees. Dr. Deshpande stated that the catalysts enjoy working with the academic grantees. He also believed that this program changes the culture of innovation. Dr. Deshpande stressed that catalysts are not on the MIT payroll because that type of association would lose the value of producing significant innovations.

Dr. Deshpande also mentioned that in 2011, the National Science Foundation (NSF) began a program that requires the investigator to apply with a mentor who has entrepreneurial experience. Investigators whose applications are accepted are put through a "boot camp" and must attend a one-hour meeting every Friday for 10 weeks to cultivate their messages about their inventions. This system helps reduce the gap between the researcher and the entrepreneur and conveys the message that there is more to success than the technology itself.

Discussion

In response to further questions about the NSF program, Dr. Deshpande explained that the NSF award program issues 50 $100,000 awards for a total of $5 million. He recommended that the SMRB refer to NSF for details about metrics or program evaluation, but he presumed that the entrepreneurial mentor must find the project worthwhile and that grants are issued quickly to allow ideas to get started.

Dr. Collins asked where the most significant cache of ideas was found: senior, mid-level, or junior staff. Dr. Deshpande explained that some professors, such as Robert Langer, Sc.D., produce numerous ideas. Dr. Langer also understands that he is not an entrepreneur, so his staff tends to leave MIT and form companies. Nurturing relevance has become a significant tool for recruiting faculty. Dr. Deshpande acknowledged, however, that a large number of applications come from younger members of the university and that graduate students in particular are very interested. Generally speaking, when a professor has an idea, he or she typically continues at MIT, whereas

post-doctoral fellows or graduate students are likely to move with the newly formed company. If it was the graduate student's or fellow's idea, they would likely become either the chief technology officer or scientific person in the company. Dr. Deshpande explained that MIT is attempting to do more to assist post-doctoral fellows in their career paths given that many will not go on to academic research.

Dr. Neil asked whether MIT's Center for Technological Innovation could be replicated or expanded to a larger scale. Dr. Deshpande responded that the desire for impact is significant, but a natural disconnect within academia about how to move an idea forward. The Deshpande Center for Technological Innovation at MIT has an executive director for a network for universities to share practices. NACIE is also working diligently on this issue; 150 university presidents have signed a letter pledging to focus on how to create an impact with research dollars spent within their campuses. Dr. Deshpande remarked that the U.S. is still ranked number one in innovation entrepreneurship, but this course of action is needed to maintain leadership for the next 20 years. He noted that many people worry that science is becoming less rigorous, but he does not believe that is the case, just that its relevance must be emphasized.

Dr. Omenn remarked on the value of learning from failures and asked whether there is a systematic way that can be done. Dr. Deshpande replied that when a project begins, there should be clear ideas of the risk involved and the thesis to be proven. Homing in on promising ideas helps alleviate risk by attempting one idea and either succeeding or failing quickly, thus shortening the experimentation cycle.

Dr. Shurin acknowledged the importance of the recent NACIE letter and agreed with the concept but noted that it is important to define relevance to tap into community innovation. The National Heart, Lung, and Blood Institute is currently attempting to understand why progress has not been made in specific areas. Dr. Shurin noted that attempting to solve a problem helps people realize what barriers exist. Dr. Deshpande responded that serendipity will always be a fluctuating point of the equation but that bringing communities together—in this case entrepreneurs and research scientists—works to overcome barriers. He also stated that bringing together these communities cannot be an arranged marriage but should be more like natural selection. The key is to make them available to one another.

Mr. Augustine stated that a number of studies have found that successful ideas are most likely to come from people who deal directly with a customer. The second most likely setting is the laboratory; the least successful location is headquarters. Dr. Deshpande explained that they are seeking breakthroughs as opposed to incremental changes or improvements, in which case there is not a direct need to connect with the user. He gave the example of a professor in Florida who developed a 3D camera to perform fluid dynamics research. He attempted to find other markets for the camera, including airport security, and finally found that dental imaging was the proper market. Facilitating innovation can involve speaking with people in different markets and asking what problems they want solved to spark ideas. The end user is not needed, but knowledge of any challenges is. Dr. Omenn noted an interesting concept implemented by the RARE Project, which connects donors and scientists.

Hon. Goldin expressed concern for the future of inspiration-driven research, wherein there need not be a specific outcome or goal. Dr. Deshpande clarified that some scientists should continue to explore core ideas without concern about relevance. However, many scientists seek a way to make

significant contributions to practical problems, and they are impeded by a faulty supply chain. He advocated finding a way to allow these inventors to have a more immediate impact. Hon. Goldin asked whether the community dedicated to relevance could be asked to support inspiration-driven research; Dr. Deshpande said he was confident, based on 10 years of experience, that intellectual pursuit would not be compromised by funding streams for impactful research.

Panel III Discussion—Strategies for Increasing Commercialization
Moderator:
Roderic Pettigrew, M.D., Ph.D., *SMRB Member*
Panelists:
Gururaj "Desh" Deshpande, Ph.D., *Co-founder, Deshpande Center for Technological Innovation*
Kevin V. Grimes, M.D., M.B.A., *Co-director, SPARK Translational Research Program at Stanford University*
Lisa M. Kurek, M.S., *Managing Partner, BBC Entrepreneurial Training and Consulting, LLC*
Rosibel Ochoa, Ph.D., *Executive Director, The William J. von Liebig Center for Entrepreneurism and Technology Advancement, University of California, San Diego*

Dr. Pettigrew reviewed a graphic depicting the challenges of commercialization, including problems with net cash flow and lack of access to funding sources (such as SBIR/STTR, friends and family, angel investment, and venture capital). The sequence of discovery, proof of concept, research and development, prototype, scale-up and manufacturing, and sales and distribution must be successfully navigated. The panelists, who are from academia and private industry, have been asked to identify challenges faced in moving promising biomedical products through the discovery and investment cycles. They also have been asked to discuss strategies and best practices for increasing the commercialization of biomedical products and to consider the role of NIH SBIR/STTR programs in the commercialization pipeline for biomedical products.

Kevin V. Grimes, M.D., M.B.A.
Co-director, SPARK Translational Research Program at Stanford University

Dr. Grimes introduced himself as the co-director of the SPARK Translational Research Program at Stanford University. He explained that the SPARK program was designed to help inventors breach the chasm between the bench and the bedside. He noted several barriers to bringing inventions from academia to the public. Faculty members tend to be extremely specialized and lack knowledge and experience in drug development, and incentives within the university are currently based on publication and grants, not on moving an invention through the validation process and into clinical trials. Funding for applied technologies is more difficult to acquire, though Dr. Grimes is hopeful that positive changes are occurring on that score.

Dr. Grimes explained that SPARK is in the Office of the Dean of the Stanford Medical School and is designed to generate proof of principle. Its mission is to educate faculty, fellows, and graduate students on translating academic discoveries into drugs or diagnostics that address real clinical needs, advance promising research discoveries to the clinical and commercial sectors, and create efficient and cost-effective approaches to discovery and development. The program attempts to help academicians overcome the obstacles involved in moving research innovations from the bench to the bedside.

Dr. Grimes reviewed the selection criteria for SPARK, which he considered basic and simple. The invention must be a therapeutic or diagnostic for any clinical indication that addresses an unmet need. Novel approaches are encouraged. Ideally, the technology would advance to the commercial or clinical sector within two to three years. Lastly, special consideration is given to orphan and neglected diseases.

The selection committees for initial applications to SPARK include some academic faculty but are primarily composed of individuals involved in local biotechnology firms. Applications are typically from technologies reported to the Office of Technology Licensing and from across the country. Applications are kept short, with a maximum length of two pages. The 20 finalists give a 10-minute pitch for their invention to the selection committee, and 10 of those are funded for two to three years. The funding levels are generally modest, in Dr. Grimes' estimation, at $50,000 per year. Milestone accomplishments are monitored, and additional money is released as each milestone is accomplished. Quarterly reports are required for program participation.

SPARK also provides education in the form of a required, yearlong seminar designed to address drug and diagnostic development. A patent review is performed at the beginning of the process to protect intellectual property. Local biotechnology venture capital experts and Stanford faculty provide mentorship, allowing SPARK to encourage match-making between the inventors and potential investors or collaborators.

Dr. Grimes explained that the industry mentors are involved for entrepreneurial opportunity, but they also enjoy the process. Of the approximately 50 industry mentors who are currently participating, at least 25 attend the weekly seminar series.

Dr. Grimes explained that the program instills the skills needed for managing projects, creating a target product profile, and generating funding. It also supports a graduate studies course on drug discovery and development. This support through access to facilities, mentorship, and introducing investigators to potential partners is intended to lower barriers toward commercialization.

Over the past six years, SPARK has supported 60 projects, of which 33 are active. Topics include global health and pediatric-specific technology. The intent is to cultivate technologies to the point that they are attractive to private investors or industry. There is also the potential for internal development through investigator-initiated trials for re-purposed drugs. Metrics of success include advancement to clinical testing, licensing, follow-on grants, publications, and increased education of faculty, fellows, and graduate students. Many of the projects that have graduated from the SPARK program have received follow-up support. Of the 27 completed projects, 10 have been licensed and seven have progressed to clinical testing. Four of the seven clinical technologies are unlicensed. Dr. Grimes provided an example of one SPARK project that repurposed a drug as a topical inhibitor of the Hedgehog pathway for treating basal cell carcinomas and basal cell nevus syndrome.

Dr. Grimes acknowledged the marked decrease in venture funding for new biotechnology companies and noted that the cost of later stage development is typically too high for academia. He noted that three SPARK projects are on hold as a result of this challenge. Programs like the global health initiative, which provides additional funds to supported universities, enable academia to take an expanded role.

Lisa M. Kurek, M.S.
Managing Partner, BBC Entrepreneurial Training and Consulting, LLC

Ms. Kurek informed the SMRB that she was trained as a biomedical engineer and moved into marketing and sales, where she learned a great deal about startup companies. She began her current business to assist new entrepreneurs in starting the process of creating a biotechnology company, including how to apply for SBIR/STTR funding.

She noted that her company, BBC Entrepreneurial Training and Consulting, is located in Michigan, which has a life science corridor comprising both the University of Michigan and numerous startup companies. Through the assistance of state competitive programs, BBC Entrepreneurial Training and Consulting is now in its 10th successful year of assisting entrepreneurs with commercial and SBIR funding applications. Through a combination of training and experience, the company is able to help companies "fill the gap" in funding; it now works with companies in 18 states. Ms. Kurek stressed that her company does not perform grant writing but rather assists with strategizing about how to acquire funding. This includes providing assistance on commercialization plans. She also helps companies apply for the Federal and State Technology Partnership (FAST) Program, through which Michigan provides matching funds to SBIR/STTR grantees to educate and train technology companies.

Ms. Kurek acknowledged that the different SBIR procedures for each NIH Institute and Center (IC) can be confusing. She echoed the sentiment that the time frame for awards is too long; in her experience, the average time from application to award is 12 to 14 months. She expressed belief that the review process is robust but noted that not all review panels consistently use the criteria for SBIR awards. Ms. Kurek agreed with previous panelists that the commercialization plan should have more emphasis during the review process. In her view, assessment of the viability of the commercialization plan should be a required part of the review process.

Rosibel Ochoa, Ph.D.
Executive Director, The William J. von Liebig Center for Entrepreneurism and Technology Advancement, University of California, San Diego

Dr. Ochoa introduced herself and acknowledged that many of the main points in her presentation are similar to those mentioned by other panelists. She stated that The William J. von Liebig Center for Entrepreneurism and Technology Advancement at the University of California, San Diego, was established 11 years ago with the goals of accelerating transfer of university discoveries to the private sector, preparing students for the entrepreneurial workplace, and increasing collaboration between the university and industry. Previously, many academic faculty members did not consider the patent process, and the Center is trying to change that culture. Its approach is to combine proof of concept with a sound commercialization plan, increasing technologies' value and potential for commercialization. Dr. Ochoa explained that proof of concept is defined as demonstrating technical performance and market feasibility. Proof of concept is achieved through mentorship and grant funding that is disbursed based on milestone achievements.

The Center typically disburses $50,000 to $100,000 in funding for each applicant. In addition, the center provides four graduate-level courses on technology commercialization and entrepreneurism for scientists and engineers, and it has created a forum to gather innovators, entrepreneurs, mentors, and scientists.

Dr. Ochoa briefly explained the Center's process for technology screening, which is refined every year. The Center, in partnership with a sponsor, identifies a need, issues a board solicitation, assigns a business advisor, conducts a phase screening project, and presents finalists to a panel of experts for review. Selection criteria are based on competiveness and size of the market, relevance to the proposed project, impact, and commitment to faculty or student success. The advisors and investigator jointly develop a technology demonstration plan, and M.B.A. students conduct market

research. Dr. Ochoa showed a schematic depicting the Technology Acceleration Program selection process, from lab discovery to final opportunities for additional partnerships or funding support (such as SBIR/STTR), and the relative time frame. Since 2006, the Center has conducted six regional Technology Acceleration Programs; focuses have included clean technologies, renewable energy, wireless health, and low-cost health care solutions. The center partners with numerous companies and government agencies, including Qualcomm, Booz Allen Hamilton, the California HealthCare Foundation, and the U.S. Department of Energy. In 2011, the center received 163 applications from 13 institutions and disbursed $1 million in proof-of-concept grants. One of the programs was highlighted in a white paper by Booz Allen Hamilton titled "Accelerating Commercialization of Cost-Saving Health Technologies" in May 2012.

To date, Dr. Ochoa reported, 1,000 students have participated in education on entrepreneurism, more than 150 faculty members have benefited from business mentoring, more than 110 innovation teams received $5 million in grants and mentoring, 36 startup companies have been supported, more than $150 million has been raised by startup companies, and more than 200 jobs have been created. Dr. Ochoa provided the example of InflammaGen Therapeutics, which received $150,000 in gap funding, business mentoring, and assistance with university processes. The William J. von Liebig Center for Entrepreneurism and Technology Advancement also supports entrepreneurial students with gap funding, graduate courses, and mentoring.

Dr. Ochoa reviewed the recommendations the Center provides to inventors who apply for SBIR funding. First, a full commercialization plan is strongly recommended. Applicants should have a clear concept of why their invention is superior, which requires thorough knowledge of existing technologies. Lastly, inventors should assemble a knowledgeable team with a thorough understanding of the problem and how they intend to solve it.

Dr. Ochoa reviewed lessons learned and best practices. She noted that researchers have little knowledge about commercialization and the complexity of the health care market, and they should be encouraged to seek expert advice. The Center strives to leverage resources by developing targeted programs that bring together stakeholders and innovators. She noted that there can be duplication in problem solving and that an active referral network or portal that addresses common problems would be advantageous. She emphasized the importance of bringing together innovators with entrepreneurs early in the process and of providing entrepreneurial education to researchers before or during the funding period. Dr. Ochoa believed that including M.B.A. students on innovator teams was an important aspect of the process and that researchers need business-oriented guidance on technology validation. A well-structured, market-oriented process that selects the best candidates is critical. Grant payments must be tied to achievements to ensure proper use of funds and technology advancement. She also stressed that faculty should not be expected to start companies and that younger staff and students are eager to meet this need. Lastly, the Center strives to continually leverage the ecosystem surrounding the university to aid technological advancement and commercialization of university innovations.

Discussion

Dr. Deshpande remarked that each panelist touched upon a similar theme: To bridge the gap between invention and market, we must either make more resources available or have more success. He expressed the view that the biggest effect will come from preparing the ideas that can

be most successful. Access to capital is a necessity for every invention. Promising ideas should be visible to entice investors.

Dr. Omenn asked whether NIH requests for proposals list in detail the points of impact that are considered high priority; Dr. Shurin responded that most ICs have funding opportunities with targeted needs. Dr. Omenn suggested the use of web sessions as a venue for hosting question and answer sessions for applicants.

Dr. Deshpande suggested that angel investors be encouraged to invest in key priority areas because they are one of the best resources available in the U.S. Co-investing with angel investors could allow inventors access to entrepreneurial success and allow relevance to help drive advancement and make it more rigorous.

Ms. Kurek noted that the NSF phase I and IIB SBIR applications prioritize matching funds from angel investors or other sources to encourage applicants to seek private funds. NSF also has a program called Innovation Corps that requires a three-person team with different strengths, including an entrepreneurial lead who is typically a postdoctoral fellow; faculty are not allowed to be the lead. It is anticipated that at the end of the program the lead will move with the newly formed company.

Dr. Collins acknowledged these approaches and noted that NIH's situation is somewhat unique in that 23 ICs administer SBIR/STTR programs at NIH. He stated that NIH is considering ways to streamline its processes but will seek to preserve special areas of interest without causing confusion or duplication. Ms. Kurek complimented NIH's SBIR/STTR funding program but admitted that many novice applicants do not understand the omnibus solicitation. A significant part of her job is guiding new entrepreneurs through the SBIR/STTR funding process. She suggested conferences as a way to expand outreach. Dr. Portnoy agreed and acknowledged the reduction in outreach due to lack of funds. He believed that SBIR/STTR should target underserved states and populations and expressed the hope that, in the future, the NIH SBIR/STTR program will do more in-person and Web-based outreach.

Ms. Kurek expanded on an earlier comment to note that one of the investigator-initiated solicitations is a 130-page document. Each IC creates its own list of priorities, which can be confusing to the uninitiated. Dr. Portnoy acknowledged the challenge and noted that the NIH SBIR Web site is being updated to be compliant with SBIR.gov, which will eventually allow applicants to review a government-wide list of solicitation information.

Hon. Goldin noted that this was the first time that use of the Web had been mentioned at the meeting and asked whether something like the Web site Kickstarter would be appropriate for fund-raising. Dr. Deshpande noted that, prior to the JOBS Act, it was not possible to raise money as equity without a qualified investor. He noted that the new mindset is that funds less than $1,000 can be raised collectively. The Federal Communications Commission is currently considering the topic for formal comment. Dr. Deshpande expressed hope that this type of fundraising could become part of the funding process for startup companies. Currently, a charity or company buys the product up front. Ms. Kurek added that she had recently attended a meeting at which an angel investor was passionate about crowdsource funding for the life sciences. Hon. Goldin remarked that NIH should remain aware of these changes and consider SBIR combined with Web-based fund-gathering as a way to multiply funds. Dr. Deshpande agreed that the concept has merit but worried that one story

of an individual losing his or her retirement could ruin the concept. Consumer protections should be put in place.

Mr. Augustine asked the panelists for their opinions on how NIH could shorten its funding time frame. Ms. Kurek responded that NIH's system is unique; it has flexibility and selective funding and can anticipate what applications will be reviewed. In her experience, applicants to NSF know within six months whether they will be funded and have the money in seven months. It was noted that the time frame for notification of award is considerably longer at NIH, and grants management can cause further delay before the money is granted. Dr. Omenn added that it is not uncommon for applicants to undergo more than one round of submissions. Dr. Deshpande acknowledged that the turnaround time for awards is extremely important. The Department of the Treasury and the Department of Commerce attempt to fund young companies within 90 days. The patent office has a "fast-track" option that takes 12 months. Dr. Deshpande believed that any measure that forces the answer, whether it is positive or negative, adds value.

Mr. Schmidt commented that the patent office has a significant backlog and that the fast-track option requires an additional fee. He believed the tradeoff for the fast-track route was significant because of the way the argument must be framed; these patents tend to be less broad, which means value may be lost. With respect to commercialization, he stressed that SBIR applicants need support to make their technologies FDA ready. He also suggested matching SBIR set-aside percentages with funding from the NIH budget to expand NIH's assistance in translating discoveries to the marketplace.

Dr. Collins asked the panelists to describe the types of applications that are most successful and the demographics of the applicants. Dr. Grimes replied that the quality of applications is good and that younger and mid-career applicants are more efficient at moving forward with their technologies. The gender and diversity spread reflects the population of the university. Ms. Kurek responded that the majority of successful applicants are male faculty or students. BBC Entrepreneurial Training and Consulting formed focus groups to assess why females were less likely to apply and found that women generally were not aware they were eligible to compete. Issues of access were also noted.

Dr. Portnoy commented that NIH has an option to shorten the SBIR phase I and II process through a fast-track application, but it is extremely competitive. Successful projects tend to have significant preliminary data. The criteria for transitioning from phase I to II in the fast track are straightforward, and administrative staff can typically approve the transition within a matter of weeks.

Another option for expanding the solicitation is to have three awards cycles per year instead of one so that applicants do not have to wait one year to resubmit. It was also noted that applications from early rounds are held not because ICs are waiting for better applications to come along, but because they are awaiting budget approval. Applications that are on the borderline for an IC's budget are held in case additional funds are released. That flexibility is likely to go away if a funding answer is required within 12 months of receipt of the application. While companies may be informed in a timely manner that their application is declined, this new rule would prohibit NIH from funding them at a later date. The entire SBIR/STTR review cycle is currently under review.

Dr. Pettigrew summarized the key points made during the panel discussion. First, applications that include problem-driven research development should address an unmet need. Assessment of the market for any new technology is crucial. Releasing funds as milestones are achieved helps move

innovations forward toward commercialization. Finally, mentoring is an important mechanism to forge relationships and share strengths that connects inventors with investors.

Dr. Cassell added that two of the key points made by the investor panel were bringing mentors into the application process and the need for a commercialization plan from the outset. In addition, impact is a significant consideration. The three points of emphasis, she noted, are "select, connect, and direct." "Select" refers to assembling the proper team, and "connect and direct" refers to the need for access to investors and mentoring in entrepreneurial expertise. Lastly, Dr. Cassell remarked that a wide range of ideas are funded by SBIR/STTR at NIH and that impact should be a priority consideration. The ideal application would include both inspiration and relevance.

Dr. Pettigrew thanked the panelists for their input. Mr. Augustine also thanked all of the panelists who contributed throughout the meeting. He cautioned that while the conversations at the meeting were very important, the Board should not lose sight of the value of truly basic research; there is a delicate balance that must be struck between seeking knowledge about health and finding ways to use that knowledge to improve health. Mr. Augustine also acknowledged that the pace of government is different than that of business and that synchronizing their clocks would be ideal. He noted that "There is nothing like looking up at the guillotine to sharpen one's imagination."

Public Comments

There were no public comments.

Value of Biomedical Research Working Group
Gail H. Cassell, Ph.D.
Chair, SMRB Value of Biomedical Research Working Group

Mr. Augustine noted that the SMRB showed great interest the recent charge from Dr. Collins to consider the best approach to assessing the value of biomedical research and that a Working Group has been assembled to deliberate this topic. Dr. Cassell informed the SMRB that the first teleconference call on this topic will take place soon. She stated her personal belief that, given the current financial climate, government support of biomedical research is critical. NIH must be able to explain this critical need to the public and to policy makers. She noted that there are numerous reports that summarize values in lives lost or saved or through economic return. She encouraged the SMRB to think of unique approaches for communicating the value of investment in applied and inspiration-driven biomedical research.

Discussion and Next Steps
Norman R. Augustine
Chairman, Scientific Management Review Board

Hon. Goldin noted that there is a disparity between the time frame for biomedical research and the need for solutions in the patient population. Medical problems are so complex that inspiration-driven research is required to convert the acquired knowledge into relevant applications. Unfortunately, he noted, it can appear that problems are not being effectively addressed because of the time needed to find and validate new therapies. He emphasized the need to clarify and define the time scale required for scientific advancement when considering the value of biomedical research.

Dr. Somerman asked whether universities that house incubators, wherein researchers have partners for SBIR funding, are still active. Dr. Omenn commented that the University of Washington and the University of Michigan use this system to assist small businesses that sprout from research at their universities. In addition, SPARK encourages commercialization of innovation to advance the economy of Ann Arbor, Michigan.

Dr. Omenn acknowledged the frustration over funding timelines but noted that the creation of the SBIR program helped create nationwide support of biomedical advancement. He believed that the patient population is extremely patient and, at some level, grasps the complexity of the problems facing researchers. With respect to the valuation of biomedical research, Dr. Omenn stressed that imaginative framing is required. He noted that the charge to the SMRB must be carefully parsed because value and investment are not necessarily the same. The concept must be framed correctly with a fresh approach.

Dr. Yancy observed that the acceleration in commercialization being sought should not come at the expense of precision. He also stated that potential conflict-of-interest issues resulting from changes to the SBIR review process could be complicated and must be carefully considered. It is also necessary to define who benefits from marketable products. In addition, NIH should understand the qualifications, attributes, and descriptors of venture capitalists, angel investors, and other players within the scheme of small business support. Dr. Yancy cautioned that there are different audiences and that transparency will be important. Lastly, he expressed concern that changes in the SBIR system for the sake of expediency could diverge from the goal of diversity in the biomedical research space. Dr. Patterson thanked Dr. Yancy for his comments, noting that diversity and transparency are part of the SMRB's overarching framework and should be remembered.

Dr. Briggs observed that the Clinical and Translational Science Award program has application to the topics discussed at today's meeting, particularly investment in mentoring and resources for training. Dr. Shurin agreed, adding that NHLBI will be creating two or three Centers for Accelerated Innovation to build on the knowledge gained and that building public-private partnerships will be a significant part of these centers. She said the centers are modeled on the Von Liebig and Deshpande Centers.

Dr. Neil commented that today's discussion validated his prejudices for applied science, and he stressed the importance of rigor during the innovation process. Technological advancement is needed, but the most expeditious process may not be best. He added that the world needs better technology, not merely more technology. Safety should not be compromised. That said, he encouraged people not to resign themselves to a slow process and to constantly be mindful of approaches to accelerate the pace of research.

Dr. Collins stated that his understanding of the current landscape for biomedical commercialization has greatly benefited from today's meeting. He noted that it is gratifying to know that the NIH SBIR/STTR program is well received, but NIH will not be complacent and will strive to improve the process. A number of dramatic success stories were told today, and he acknowledged that NIH can do a better job telling those stories. These success stories also can serve as case studies for effective practices, and analysis of projects that were not successful will also be useful.

Dr. Collins expressed his gratitude for the work of the SMRB. With respect to deliberating approaches to finding the value of biomedical research, he noted that the end product must be a rigorous analysis that will withstand criticism. He also agreed with Dr. Neil that the community should constantly strive to improve itself, quoting the Franciscan blessing "May you be blessed with enough foolishness to believe that you can make a difference in this world so that you can do what others claim cannot be done."

Closing Remarks and Adjournment
Norman R. Augustine
Chair, Scientific Management Review Board

Mr. Augustine informed the SMRB that the next meeting will take place on January 14, 2013, on the NIH campus. He thanked Dr. Patterson and her staff for coordinating logistics for the meeting and thanked Dr. Collins for continuing to make serving on the SMRB a rewarding experience.

Mr. Augustine concluded by thanking SMRB members for their time and efforts. In particular, he thanked Dr. Shurin and Dr. Green, whose terms as active members will end soon but who will continue to serve the Board on an ad hoc basis. He adjourned the meeting at 4:06 p.m. Eastern Standard Time.