By Steve Benowitz

The cancer research community is pumped, primed, and apprehensive. On one hand, scientists have widely welcomed the Obama administration’s plan to inject approximately $10.4 billion in economic stimulus funds into the National Institutes of Health. It means more support for innovation, for enhancing current projects, for improving equipment—even for bumping up a falling NIH and National Cancer Institute pay line to enable funding of more deserving projects.

“There’s true scientific and intellectual excitement,” said Barrett Rollins, M.D., Ph.D., chief scientific officer at the Dana-Farber Cancer Institute in Boston. “There’s a lot of excitement that we’re finally getting enough money for the work we’ve been doing.” But with all the enthusiasm comes some hard economic realities. NCI was given roughly $1.3 billion of the NIH pie when the stimulus package details were announced in February—and little time to figure out how to spend it all in only 2 years. Research and grant offices worked overtime and weekends at cancer centers across the country from the time of the NIH stimulus package announcement to the grant submission deadlines, particularly for Challenge Grant applications, which will support projects in specifically defined research areas. Often, grant offices read and digested NIH and NCI materials and summarized them into meaningful and sometimes even daily directives for faculty and staff. Researchers sometimes had only weeks from the time of the NIH announcement to cobble together grant proposals. NIH, on its end of the funding pipeline, had to reinvent a proposal review system to meet the demand.

The funding opportunities come in various shapes and sizes. The stimulus package will pay for several types of grants: the Challenge Grants; Grand Opportunities Grants aimed at short-term, large-scale research projects by multidisciplinary teams; supplements to expand existing funded research projects; funds for those high-scoring proposals that missed last cycle’s funding cut; infrastructure improvement of research facilities; funds for scientific equipment; and more than $400 million set aside for NIH comparative effectiveness research, which compares the benefits of various therapeutic approaches.

With an overarching goal of stimulating the economy and creating jobs, many say that the opportunities offered by this stimulus package come not a moment too soon. “Once the NIH budget doubling stopped 6 years ago, we’ve had to increasingly rely on foundations and philanthropic contributions,” said William G. Nelson, M.D., Ph.D., director of the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins in Baltimore. Because NIH purchasing power plummeted 13% in that time, “increasing the funding pool makes a lot of sense.”

Many researchers say that the most attractive of the opportunities is the Challenge Grant, which is for 2 years and $1 million. With little if any preliminary data required, unlike R01s, Challenge Grants are designed to jump-start new areas of research in 15 broad scientific areas such as translational science, genomics, clinical trials, health disparities, and behavioral change and prevention. Yet there’s a downside as well. NIH has allotted only $200 million of its $10 billion pot for 200 Challenge Grants, and with more than an estimated 20,000 applications in NIH’s mailbox at the April 27 deadline—approximately the number of applications NIH receives in one of the agency’s three major review rounds each year—the pay line would be approximately 1%.

“It’s a testimony to the hunger of the scientific community for opportunities to do innovative research,” said Louis Weiner, M.D., director of the Lombardi Comprehensive Cancer Center at Georgetown University in Washington, D.C., who submitted three grants himself.

Karen Messer, Ph.D., director of bio-statistics at the Moores Cancer Center at the University of California, San Diego, is hoping to take advantage of the opportunity. Messer, who said that the prospect of new funding “has had a huge cheering effect on the research community,” submitted a proposal to integrate patient tissue and blood samples from a cancer center biorepository with electronic medical record data.

Messer noted that writing a Challenge Grant application “was as much work as putting in an R01 for 5 years.” Even if hers isn’t funded, she said, she and others can always, and many are already planning to, resubmit the 2-year proposal as a 5-year R01 grant request. She said that many have done the opposite—recycled previously rejected R01 proposals into Challenge Grant applications.

The prospect of intense competition has not dissuaded many. Rollins said that
Dana–Farber submitted more than 120 stimulus grant applications. J. Robert Beck, M.D., senior vice president and chief academic officer at Fox Chase Cancer Center in Philadelphia, noted that of 90 principal investigators, 28 applied for grants. Beck put in a Challenge Grant application for a health information system for radiology imaging. Although it probably would not have been funded normally, he said, it’s the type of “out of the box” grant application that was encouraged.

**Strategic Planning**

Many cancer centers have tried to take a strategic approach to their grant applications. Hopkins’ Nelson said that the Kimmel Comprehensive Cancer Center officials tried as much as possible to look at where they thought stimulus package funds could best help them. One area was in recruitment. Applications for 2-year administrative supplements, for example, were aimed at certain areas they were trying to recruit for and would entail a matching 2-year commitment from Johns Hopkins. The cancer center applied for 67 grants in all, including 20 Challenge Grants and 21 administrative supplements. Individual researchers drove the applications for Challenge Grants, Nelson said, but at the same time, “we asked, is this strategically a direction that we could support and take advantage of in 2 years?”

Dennis Carson, M.D., director of the University of California, San Diego’s Moores Cancer Center, would like to see investments in broader projects. The Moores Cancer Center emphasizes translational oncology and drug development. Carson said that because of the millions of dollars it takes to find out whether a drug works, he’d like to see some funding pointed to programs that develop early-response criteria for drug testing, including imaging and biomarkers.

Like other cancer center directors, Carson and his team also steered cancer center stimulus fund proposals toward strategic goals, such as needed recruitment, investigator-initiated trials, and the creation of a protocol development office.

“I think that these could be more important investments than individual Challenge Grants,” he said, lamenting their limited 2-year shelf life and 1%–2% pay line. “I think that the Challenge Grants are a mistake because in most cases we’re not going to be able to complete a project in 2 years, and then what?”

He thinks that the Grand Opportunities Grants and administrative supplements are much more fruitful to the entire cancer center and research in general. “Grand Opportunities Grants enable scientists from varied backgrounds to collaborate, with people who speak different languages actually talking to one another and exchanging ideas,” said Carson. “That’s how science advances.”

Rollins agreed. “GrandOpportunities Grants have already created new and interesting collaborations that otherwise might not have occurred,” he said. Likewise, competitive revisions to modify existing grants “were a great idea because they address a longstanding underfunding situation in many areas.”

**Costs and Benefits**

Michael A. Caligiuri, M.D., director of the Ohio State University Comprehensive Cancer Center and CEO of the James Cancer Hospital in Columbus, Ohio, sees both costs and benefits in the stimulus package.

On one hand, Ohio State’s cancer center has submitted more than 70 proposals and has already heard that it is receiving funding on a resubmitted proposal of about $8 million to support construction of a biomedical research building on campus.

“The new building construction will employ at least 25 new principal investigators, with another five to six people per lab, meaning at least another 100 jobs bringing in federal funding and adding millions in direct economic impact to the region,” he said.

Ohio State has also applied for equipment grants, including deep sequencers that can unravel the codes of large amounts of DNA in short periods for its human cancer genetics program. “It’s a strategic opportunity for us,” Caligiuri said.

But Caligiuri echoed the frustration about the low Challenge Grant pay line. “Researchers and administrators did nothing but work on Challenge Grants for weeks and not on their research, teaching, and clinical care,” he said. “If you are trying to stimulate the economy, we need to fund many more than 2% of the Challenge Grants, as is currently planned. It’s very troubling because I’m asking my people to slow down everything for a small chance of a payoff.”

Early-career investigators also had some concerns about whether applying for Challenge Grants is worthwhile. Although NIH relaxes the rules for young investigators who have not yet received an R01, winning a Challenge Grant can affect this protection.

Marcia Brose, M.D., Ph.D., assistant professor of hematology–oncology at the University of Pennsylvania School of Medicine and Abramson Cancer Center in Philadelphia, could fall into this category. She has not been able to get an R01 and has applied for two Challenge Grants (one aimed at planning clinical trials of thyroid cancer, whereas the other is on the role of aromatase activity in BRCA1–related breast cancer).

Brose said that the stimulus funds are available for early investigators who are less than 10 years into their careers; a
special extension has allowed her to just qualify. But she’s pessimistic about her chances and worries about the anticipated jump in unfunded Challenge Grants turned R01 applications. “There’s a group of us who have hit the sweet spot of funding shortfalls, and there will be a generation of researchers missing,” she said. “We’re hoping stimulus funds help.”

The Challenge Grant challenge aside, some wonder if cancer center infrastructures will be up to the task.

“One of the challenges we conceivably face is that as our investigators tap into these resources to move their own research forward; the cancer center infrastructure may not have the same flexibility to expand to accommodate that additional demand,” Georgetown’s Weiner said. A researcher, for example, gets a Challenge Grant and needs to ramp up his activity in a shared resource—and that resource isn’t available. “It’s a partially unintended consequence and it could be a problem for those who are particularly successful in securing these grants. Resources may not be sufficient to accommodate the research that needs to be done.”

Nelson said he thought that larger cancer centers were best equipped to take advantage of stimulus package funds in the longer run. “These are the types of grants that we could conceivably build and grow a program around,” he said. “It’s a sort of multiplier effect. We could leverage funding from other sources as well to build on something.

Future Questions

Awards have been trickling in. And thanks to a nearly 3% increase in NCI funding for the new fiscal year and a resulting rise in the NCI pay line from 12% to 16%, some researchers have had good news. Two Johns Hopkins scientists, for example, already have heard that their previous grant applications, initially unfunded, were approved. Still more will come when funds from the stimulus package are added and the pay line increases to the 25th percentile (grants falling in the 18th–25th percentile will be a mix of 2- and 4-year projects). Already, some have had good news.

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In the wake of receiving part of the $10.4 billion slated for the National Institutes of Health from the American Recovery and Reinvestment Act of 2009, the National Cancer Institute director John E. Niederhuber, M.D., and his staff immediately began to outline what is necessary to allocate their $1.26 billion chunk.

First, wade through thousands of applications from grantees, all vying for a piece of the pie. Second, award the best of the best so that funds are injected into promising projects that also help invigorate a weak economy. And finally, make it happen in a relatively short 2-year time frame.

With all this on his plate, it’s no surprise that the NCI director characterizes his position lately as “all time consuming.”

In discussing the plans, Niederhuber noted, “Moving from data to function to target to therapy will not be simple, nor will it be inexpensive.” Still, with the new funds, there are “areas of investigation that are uniquely in position to accelerate discovery in a short number of years,” he said.

Tapping his pen occasionally, he talked in his 11th-floor office in NIH’s Building 31 about how this influx can pave a research path that could make substantial inroads toward eventually overcoming the disease. “It makes a lot of sense to use the stimulus dollars to jump-start this,” he said.

JNCI: How do you see NCI’s role in using the new stimulus funds? And for you, what’s the “big picture” in all this funding?

Niederhuber: I don’t think this is a time to be timid; we have to grab hold of this—not just keep pouring money down the same things we’ve always been doing.

This is a painful disease. There isn’t any one of us that isn’t either going to be told we have cancer or that somebody we really love—husband, wife, or parent—isn’t going to be told. We’ve got a major problem of pain in our country.

There is an increase in our budget and we are beginning to work more intensely on what is it the people of our country want us to do.

JNCI: One of the “signature” projects to be used with this funding is expanding The Cancer Genome Atlas (TCGA) project. [This project is studying genetic changes associated with the development of many cancer types, including lung, ovarian, and brain cancers.] What, generally, is the basis for this research?

Niederhuber: Let’s keep the patient always as the reference point. And how do we get there? By understanding the basis of the disease, and it’s clearly in the altered genetics, in the genome. We start by cataloging what are the things that are wrong—that lead to cancer.

We’ll design two or three mechanisms to optimize, to really understand, what the genetic catalog means—the cellular communication and biologic function. Once you know that, then you can go look at that. Here’s where we can attack …

JNCI: What is the importance of the catalog?

Niederhuber: It’s got a ton of information. We’ve got to build the tools and bring in the right people to analyze this. And that will help us fill in the gaps in terms of understanding what are the defects in terms of biologic function, how the signal pathways change.

JNCI: In another signature project, NCI is using stimulus funds to explore new and innovative approaches to better understanding and controlling cancer, such as building a collaborative network with the physical sciences.

Niederhuber: As I looked at the scientists working on cancer, it struck me that we had never gotten into the physical sciences, the physicists, and the people who study mathematics and applied mathematics—even people in physical chemistry.

We got 37 applications for this and among those were seven Nobel laureates. I don’t know what will come out of that … but I bet something exciting.

JNCI: NCI brought together leaders from the physical sciences last year for a series of three think tanks to brainstorm about cancer research. How did that go?

Niederhuber: You know, looking at this disease through a different lens was eye opening: These were three of the most exciting meetings I’ve sat through in 40 years. They talked about things I didn’t know about, like communication theory, evolutionary biology. It was a very exciting time.

JNCI: The burden of cancer has touched you.

Niederhuber: I lost my wife and best friend to breast cancer. It is all-consuming now, thinking how we can move ahead, move forward with the resources we have to fight this disease.

— Joseph Cantlupe
grants, not all of which will come from stimulus sources).

These increases notwithstanding, many are concerned about the poststimulus era and what the cancer research world will look like when the money runs out.

“The big unasked question in regards to the $10 billion is sustainability,” said Fox Chase’s Beck. “The Obama administration, Sen. Arlen Specter (D-Pa.), and others have said they recognize that this is only a short-term fix to stimulate research.” He noted that President Obama has said that he would like to see current research dollars increase in his term, and Specter would like to see a trajectory in research spending rather than simply the flat spending of the last several years. But whether increased investment will follow the stimulus package in the next four years remains to be seen.

“We won’t know how effective this approach will have been for another few years,” Weiner said. “The 2-year timeline doesn’t fit comfortably in the timelines of most cancer centers.”

Rollins is also concerned about the future. “The single biggest challenge is what to do with the fact that the funding only lasts for 2 years,” he said. “We’re already having discussions about that. As we get awards, we will have to hire people, but what will we do after 2 years? The government is betting that the economy will improve in 2 years and absorb this increase. I worry about whether the money will be there and what will happen.”