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NCI to Spend $70M on Precision Oncology In Presidential Initiative, Even if Congress Doesn't Appropriate New Funds, Varmus Says

By Conor Hale

NCI will implement President Barack Obama's directive to ramp up the initiative in precision medicine, even if Congress doesn't appropriate specific funds for this purpose, Institute Director Harold Varmus told members of the National Cancer Advisory Board Feb. 12.

The White House budget proposal for fiscal 2016 includes $200 million for NIH to spend on the Precision Medicine Initiative. On top of that, the proposal includes a 3.2 percent overall budget increase.

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Tufts Researchers Say Blood Cancer Drugs Are a Good Value; Kantarjian Disagrees

By Paul Goldberg

Even at high cost, blood cancer drugs provide a good value, an analysis by Tufts Medical Center researchers found.

In a paper published online by the American Society of Hematology journal Blood, the Tufts team presents data from a meta-analysis to argue that, even considering their cost of $100,000 or more a year, targeted therapies, as they translate into years and quality of life gained, may justify the prices.

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MD Anderson Pediatrics Chair "Resigned" To Pursue Academic Interests—Or Did She?

By Paul Goldberg

According to MD Anderson administration, Eugenie Kleinerman "decided to step down as Head, Division of Pediatrics, and Chair, Department of Pediatrics, effective Feb. 9 in order to pursue her interests in new initiatives in adolescent and young adult cancer."

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Precision Medicine Initiative Set to Officially Begin Oct. 1

(Continued from page 1)

For NCI, this would mean a $70 million boost for precision medicine in oncology—some on work that's already underway, Varmus said.

The president's version of the budget was delivered to Congress, which has to act to deliver its own budget that appropriates funding and authorizes spending (The Cancer Letter, Feb. 6, 2015). Whatever happens, Varmus said, the institute would move toward the president's goals.

"The NCI is committed, of course, to fulfilling the president's desire to have $70 million spent on this initiative. And we will do that," Varmus said to the board in his opening remarks. "There is no guarantee that we will have the funds from Congress to explicitly do this.

"In other words, there are two things about the appropriations process this year that will be interesting to watch.

"The first is whether we the NIH will receive the increase in overall spending the president has requested, and secondly whether the Congress will actually place some kind of highlighting on the Precision Medicine Initiative. There has been a tendency that you may have noticed, for this Congress to not necessarily go along with every request that has been submitted by this president. I think it will be interesting politically to watch."

Cover Photo: NCI Director Harold Varmus addressing a joint meeting of the NCAB and the Board of Scientific Advisors Dec. 2.

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NCI has been devoting considerable resources to precision medicine, Varmus said.

"The $70 million that is designated to the NCI for work on precision medicine in oncology is, I would argue, closer to launch—in fact many of the things we plan to do with the $70 million are already underway, and those efforts represent an acceleration or expansion of activities already in motion."

Varmus said the spending would be concentrated in several areas:

"One is an expansion of our efforts in genomics. Obviously we're already fairly productive, but we'll be extended in certain ways. The genomic information and technology will be applied with increasing vigor to a series of trials exemplified by the MATCH trial that's been much discussed, but not yet launched, and will be conducted by the National Clinical Trials Network."

The funding will also supplement efforts in matching therapies to particular cancers on the molecular level, dealing with drug resistance and tumor heterogeneity, and developing better preclinical models for testing drug combinations. There will also be a large informatics element, Varmus said.

About $130 million of the proposed NIH budget is designated for an upcoming research cohort study that plans to enroll over one million patients. "The nature of the cohort—the kinds of studies to be done, the duration of the study, the possible cost of it in the long run—are all under discussion," Varmus said.

A transcript of Varmus's Feb, 12 remarks to the NCAB follows:

First, [NCAB Chair] Tyler [Jacks], let me congratulate you on your reappointment as chair. And this is actually a signal event, because it means the White House is now paying attention to our nominees for the six empty slots on the NCAB—nominations that were sent to the department about a year and a half ago.

I know we have to be very careful about who's appointed to the NCAB, but this long appointment process is not a good one. I have a good friend and eager, active contact in the personnel office of the White House, and I'm sure the slate that we submitted some time ago will now be rapidly processed.

There are two things I would like to talk about just briefly: one that you've heard a lot about, and that is the president's Precision Medicine Initiative that was announced by the White House on Jan. 31, and appears in the president's proposed 2016 budget.

You'll recall that the appropriation for this year is roughly a half-percent above last year's. We're moving

in an expeditious way to put that into play and the good news for this year's budget is that we did get it in the first quarter of the fiscal year which is unusual in these parlous times, and that's allowing the NCI senior staff to make decisions about how we allocate funding for grantees and centers and so forth in a more thoughtful and expeditious way.

The president's budget for 2016 has a 3.2 percent proposed increase for the NIH overall, consistent with the general plan to try to stimulate the economy—as the economy improves, restoring funding for essentially many agencies that receive discretionary funding back to pre-sequestration levels. If Congress in fact honors the president's request, or even supersedes it, the NIH will be back to where it was in 2012, which is a good thing. Historically, that looks not quite as exciting as it might be. But under these circumstances—if we get back to those levels—I think all of us will be pleased.

In that budget, there is for NIH [$215] million that the president would like to see the NIH spend on his Precision Medicine Initiative.

Roughly two-thirds of that money, $130 million, is designated for a large study that is sometimes referred to as the cohort study, but is intended to be a lot more than that. That has not yet been precisely outlined. In fact, yesterday and today, 70 individuals are meeting on the NIH campus, including two senior members of the NCI, to discuss the possible framework and its methodology to bear on essentially all diseases by setting up and studying a roughly one-million-member cohort.

The nature of the cohort—the kinds of studies to be done, the duration of the study, the possible cost of it in the long run—are all under discussion during these two days. There will be a standing outside committee, headed by Rick Lifton [chair of the department of genetics at Yale University], that helps to oversee this process.

The $70 million that is designated to the NCI for work on precision medicine in oncology is, I would argue, closer to launch—in fact, many of the things we plan to do with the $70 million are already underway, and those efforts represent an acceleration or expansion of activities already in motion.

The activities will be overseen and coordinated by a group of internal senior members of the NCI, who have been working on this project with the White House and the rest of the NIH for the past several months.

The activities will be in four broad areas.

One is an expansion of our efforts in genomics. Obviously we're already fairly productive, but we'll be extended in certain ways. The genomic information and technology will be applied with increasing vigor to a series of trials exemplified by the MATCH trial that's been much discussed, but not yet launched, and will be conducted by the National Clinical Trials Network.

There will be other trials that were not previously planned or envisioned, including a pediatric MATCH trial and trials that are focused on certain common cancers.

There will be a series of efforts made to improve our understanding of cancer biology with the specific ambition of doing a better job in matching drug therapies to the description in molecular terms of particular cancers, dealing with the problems we faced with drug resistance and tumor heterogeneity, and attempting to develop better preclinical models for testing, especially testing drug combinations.

And finally the fourth element will be a large informatics element, which has already been launched, but will be accelerated through that money. For example to increase the support for developing useful tools for managing and gaining access to the large amounts of genomic and clinical data that are being assembled through the other projects that I mentioned.

I emphasized that this is a presidential initiative. It comes with a request for appropriations—it doesn't come with appropriations—that's up to the Congress.

You may have heard that there has been a shift in the dominance of the Republican Party in the Senate, and we have new chairs for appropriations and authorizations of all our committees in the Senate.

And there is some turnover in the House. We can provide you with all those names; I'm not going to rattle them off at the moment. But there will be an appropriations process as usual. The House appropriations subcommittee for Labor, Health, and Education will meet on March 3.

I wanted to mention that this week, on Tuesday, we held a meeting of the NCI-designated cancer center directors. I thought it was a useful meeting.

It focused largely on the various aspects of sharing the facilities of the clinical center through the collaborations and training that brings the NIH Clinical Research Center together with many of our cancer centers.

There was discussion of how the cancer centers themselves can share their core facilities more readily, and a number of discussions of supplementary funding that's been used to promote the involvement of centers in global health.

The centers themselves are about to gather those centers that have taken a special interest in global health and meet together in Seattle in a couple of months.

In addition, there was some discussion of budget reallocation.

An initiative began several years ago—we've had difficulty, as I have admitted, in trying to come to a resolution on how those budgets should be allocated, taking into consideration the advice of that working group. We're hoping to take some steps forward now that we've had some discussion of what the impact of living by certain rules would be.

In addition, the center directors, and I, and my colleagues, celebrated the career of Linda Weiss as she departs as the director of the Office of Cancer Centers, [which she served as] over the last 13 years. With some fear of embarrassing her with a third day in a row of applause, let me thank her for her service to the cancer centers, one of the most important parts of the NCI. Linda, thank you very much and Tyler, thank you for your attention.

Any questions?

JACKS: I'll ask one question related to the Precision Medicine Initiative and the $70 million that may come to the NCI. You mentioned that some of the programs are already ongoing and we imagine that this money will be deployed in those directions. There are other ones that are, in my understanding, still being planned—the preclinical models, and the design of new preclinical models for new platforms for drug testing. Do you have specific ideas about how those would roll out or is it too early to say?

VARMUS: I think it's probably too early to say. We do have some initiatives ongoing already, and hoping to develop PDXs and grants for studies of organoids and cancer stem cell cultures. I think we haven't decided how exactly we're going to implement those ideas.

In our discussions with the White House and the Office of Science and Technology Policy, these were among the examples of things we proposed to do to increase the biological understanding of cancer, so that we have a better job in dealing with drug resistance and putting combinations of drugs together.

I should mention that a small part, about [$10 million] of this initiative, of the [$215] million that I've discussed, is designated for the FDA.

We've had frequent discussions with the FDA about how they're going to oversee, and in some cases regulate diagnostic testing and the use of certain tests to allow the use of certain drugs. And all of these factors—that is the development of models, the development of genomic platforms that are used for such tests, the indications for genetic abnormalities that would allow the best use of drugs and drug combinations—are all under discussion with the FDA.

This is an initiative that will officially begin in FY16, Oct. 1. So we have some time to get a little more specific about the plans. But there are some that are already in motion and will be supported in part by these funds.

The NCI is committed, of course, to fulfilling the president's desire to have $70 million spent on this initiative. And we will do that. There is no guarantee that we will have the funds from Congress to explicitly do this. In other words, there are two things about the appropriations process this year that will be interesting to watch.

The first is whether we the NIH will receive the increase in overall spending the president has requested, and secondly whether the Congress will actually place some kind of highlighting on the Precision Medicine Initiative. There has been a tendency that you may have noticed, for this Congress to not necessarily go along with every request that has been submitted by this president. I think it will be interesting politically to watch.

There is clearly Republican support for the idea of pursuing precision medicine. We've had visits to the campus not just by [HHS] Secretary [Sylvia] Burwell and President Obama to talk about some of these things, but also by six members of our newly constituted appropriations committee, including four Republicans and the new chair of the committee, [Rep.] Tom Cole (R) from Oklahoma.

And all were extremely interested in hearing about what the NCI and other institutes are doing. They spent some time hearing about immunotherapy from Crystal Mackall [head of the NCI Immunology Section and chief of the Pediatric Oncology Branch] and colleagues, and there's no doubt that this is a receptive group.

Whether they're going to give us the recommended increases, and whether they're going to highlight the president's request for emphasis on precision medicine remains yet to be determined.

Two Blood Editorials Debate Cost-Effectiveness of Drugs

(Continued from page 1)

"Given the increased discussion about the high cost of these treatments, we were somewhat surprised to discover that their cost-effectiveness ratios were lower than expected," Peter Neumann, director of the Center for Evaluation of Value and Risk in Health at Tufts and the senior author of the study, said in a statement. "Our analysis had a small sample size and included both industry- and non-industry-funded studies. In addition, cost-effectiveness ratios may have changed over time, as associated costs or benefits have changed. However, the study underscores that debates in health care should consider the value of breakthrough drugs and not just costs."

In April 2013, Blood published an editorial by a group of more than 100 experts in chronic myeloid leukemia, who sought to draw attention to the high prices of cancer drugs, with the particular focus on the prices of approved tyrosine kinase inhibitors for the treatment of CML.

"Grateful patients may have become the 'financial victims' of the treatment success, having to pay the high price annually to stay alive," that paper reads. A conversation with Hagop Kantarjian, the corresponding author on that paper and chairman of the Department of Leukemia at MD Anderson Cancer Center, appears in the May 31, 2013, issue of The Cancer Letter.

The recent Tufts paper, which appears in the opinion section of Blood, is based on a systematic review of peer-reviewed cost-effectiveness analyses published between 1996 and 2012.

The Tufts team focused on studies that examined cost utility, measured as a ratio of a drug's total cost per patient quality-adjusted life year gained.

The abstract states:

"We analyzed cost-effectiveness studies related to hematologic malignancies from the Tufts Cost Effectiveness Analysis Registry (www.cearegistry.org), focusing on studies of innovative therapies.

"Studies that met inclusion criteria were categorized by four cancer types chronic myeloid leukemia (CML), chronic lymphocytic leukemia (CLL), non-Hodgkin's lymphoma (NHL), and multiple myeloma (MM) and nine treatment agents (α interferon, alemtuzumab, bendamustine, bortezomib, dasatinib, imatinib, lenalidomide, rituximab alone or in combination, and thalidomide).

"We examined study characteristics and stratified cost-effectiveness ratios by type of cancer, treatment, funder, and year of study publication. Twenty-nine studies published 1996-2012 (including 44 cost-effectiveness ratios) met inclusion criteria, twenty-two (76%) of which were industry-funded. Most ratios fell below $50,000/QALY (73%) and $100,000/QALY (86%). Industry-funded studies (n=22) reported a lower median ratio ($26,000/QALY) than others (n=7) ($33,000/QALY), although the difference was not statistically significant.

"Published data suggest innovative treatments for hematologic malignancies may provide reasonable value."

Kantarjian said he isn't convinced by the Tufts paper.

Kantarjian and Jagpreet Chhatwal, from the Department of Health Services Research at MD Anderson, critiqued the Tufts paper in an email to The Cancer Letter.

"This analysis, spearheaded by the Institute for Clinical Research and Health Policy Studies at Tufts, implies that high cancer drug prices are justifiable," Kantarjian and Chhatwal wrote. "This is an unfortunate and misleading message.

"This well-intended analysis, as well as similar studies funded by pharmaceutical companies, appear to advocate for and justify high cancer drug prices that benefit interest groups, but harm patients. High cancer drug prices make them unaffordable and unavailable to many patients with cancers and they burden our health care system, diverting money into unreasonable profits, money that could be better invested in direct patient care or in parallel innovative research.

"The investigators combined multiple cost-effectiveness studies, whose results are highly dependent on the assumptions and parameters used in each individual study. For example, the price of drugs, time horizon, quality of life, and baseline patient characteristics all influence the conclusions of each study.

"One obvious example is the price of imatinib, which was about $26,000 in 2001, increased to $92,000 in 2012, and to a more recent price of $132,000 in 2014. The current imatinib price of $132,000 a year is the price that should be considered in measuring the drug cost effectiveness, or 'treatment value.' We cannot conclude that imatinib is cost-effective in 2014 based on 2001 drug price. By combining studies from different years and using different drug prices, the approach in this analysis is flawed, which results in the misleading message. The correct analysis should be based on the current drug price, and other assumptions.

"The unaffordable high cancer prices became

a critical issue since 2006. As discussed in previous editorials, the average price of a cancer drug was less than $10,000 a year before 2000 and about $30,000-$50,000 in 2005. Today all new cancer drugs approved by the FDA since 2012 have been priced at more than $120,000-150,000 a year. As reported by Dr. David Howard and colleagues in a recent publication titled 'Pricing in the Market for Anticancer Drugs,' the prices of cancer drugs have increased by an average of $8,500 per year. Therefore, this analysis, which considers studies mostly before 2011 (23 of 29), and incorporates older prices based on the year of publication, may reflect the 'treatment value' in that year, but do not reflect the 'treatment value' in 2014. This is what our present discussion of unreasonably high cancer drug prices is about".

"As the authors also acknowledge in the discussion, 22 of the 29 studies analyzed (76%) were funded by the pharmaceutical industry. This clearly creates a selection bias of papers and an analysis bias of the data, both tilting to reflect a positive message of 'reasonable value' for cancer drugs and to justify the current extremely high cancer drug prices.

"In addition, the drug prices in almost every country are lower than in the United States. Therefore, it would be incorrect to combine the cost-effectiveness studies from multiple countries and provide a universal message, as done in this analysis.

"The reality is that the high cost of cancer drugs emerged as an epidemic problem since the mid-2000's and has become impossibly unsustainable and morally unjustifiable in recent times.

"We need to stop justifying these high cancer drug prices and advocate for our patients who are being harmed. Our obligation as physicians is to protect our patients from harm and injustice, both being perpetuated by high cancer drug prices.

"Since most parties involved in the discussions of cancer drug prices have particular interest and motivations, we believe the only way to reduce cancer drug prices and make them available to our patients is through a patient-based grass root movement of 1 million signatures that decry the high cost of cancer drugs and their harm to many individuals with cancer fighting for their lives on a daily basis."

The Novartis composition-of-matter patent on imatinib in the U.S. was scheduled to expire in January 2015. However, an agreement between Novartis and Sun Pharmaceutical Industries Ltd., has deferred generic entry to February 2016. Generic imatinib is available in Canada and Mexico. For most European Union member countries, the patent will also expire in 2016.

MD Anderson Pediatrics Chair "Resigned"—Or Did She?

(Continued from page 1)

This was the version of events promulgated by MD Anderson Provost Ethan Dmitrovsky.

Leonard Zwelling, a former MD Anderson executive and Kleinerman's husband, offers another version.

Kleinerman did not "resign," Zwelling writes on his widely read blog.

"Nothing about this surprised me, especially the particularly sudden and unskillful manner in which it was done," Zwelling writes. "There was no warning and no discussion with the Pediatrics Division Head prior to her 'resignation.' This has not been in the works for months at least from her side.

"Second, that someone who has made major contributions to MD Anderson and its faculty should be made to feel 'less than' has become pretty common. There are others who, for one reason or another, felt less than welcomed any longer. Many have left and it is MD Anderson's loss that they have.

"The motives behind the latest purge among the Division Heads is, however, abundantly transparent. Like anything else involving [MD Anderson President Ronald] DePinho or, for that matter, the last 15 years of MD Anderson administrations, it's about the money and who gets to control it.

"It couldn't go any other way and it is not the last of the ritual public/private hangings that we can expect of various faculty leaders.

"By sitting on the sidelines as successful Division Heads were fired, department chairs left, and other faculty and non-faculty players who could get out did, the Faculty Senate sowed the seeds of the pogrom now fully operationalized at the hands of the white men who run MD Anderson.

"Sooner or later they'll come for you, too. It is just so disappointing to see it play out like this on Holcombe, but these are the seeds sown by the corrupt culture of the previous administration that supplanted the faculty- and patient-centered eras of Clark and LeMaistre. No one should be surprised. This blog certainly wasn't and might even have played a role in the whole fiasco. Mea culpa!"

The text of Dmitrovsky's announcement of what appears not to be a resignation follows:

From: Dr. Ethan Dmitrovsky
Sent: Tuesday, February 10, 2015 4:15 PM

Subject: Eugenie Kleinerman, M.D., steps down as Pediatrics Division Head/Department Chair

Dear Colleagues:

We want to share with you that Eugenie Kleinerman, M.D., has decided to step down as Head, Division of Pediatrics, and Chair, Department of Pediatrics, effective February 9th in order to pursue her interests in new initiatives in adolescent and young adult cancer. Dr. Kleinerman is internationally recognized for her scientific and clinical expertise in sarcomas, particularly osteosarcoma, and we are fortunate that she will continue her scholarship as Professor of Pediatrics and Cancer Biology.

We are pleased that Cindy Schwartz, M.D., has agreed to serve as Division Head *ad interim* and Department Chair *ad interim*. With an impressive career built at the University of Rochester, Johns Hopkins and Brown University, Dr. Schwartz joined our faculty in 2013 as Professor of Pediatrics and Deputy Division Head of Pediatrics.

Dr. Kleinerman joined MD Anderson in 1984 as an Assistant Professor of Pediatrics, with a joint appointment in Cell Biology. She rose through the academic ranks, earning the rank of Professor in 1993. In 2001, she was named Division Head and Chair of Pediatrics.

One of Dr. Kleinerman's crowning achievements is taking a new treatment concept from hypothesis through laboratory and animal investigations to multi-phase clinical trials that led to regulatory agency approval. She pioneered the use of a unique immunotherapy agent, liposome-encapsulated MTP-PE, for children with unresponsive, relapsed osteosarcoma lung metastases. With the approval by European Medicine Agency, liposomal MTP-PE (Mepact), now is available in 27 countries. This represented the first improvement in long-term survival of children with this disease in over 20 years.

Dr. Kleinerman's work has led to more than 170 articles and 21 book chapters. She has served on numerous NCI study sections and was a prior member of an FDA advisory panel.

During her leadership tenure, Dr. Kleinerman recruited a cadre of stellar faculty and increased the translational and clinical research within the division. The pediatrics fellowship program has been greatly expanded into a robust and highly competitive program. Under her leadership, the research training program for clinical fellows was established. As evidence of the elevation of pediatrics care at MD Anderson, the Children's Cancer Hospital was initiated, as well as many supporting efforts such as Kim's Place, an activity center in The Park for adolescents and young adults.

Please join us in thanking Dr. Kleinerman for her 14 years as Division Head and Department Chair. Please also thank Dr. Schwartz for her expanded service. We are confident she will provide the leadership needed during this time of transition.

Sincerely,

Ethan Dmitrovsky, M.D., Provost and Executive Vice President

Thomas Buchholz, M.D., Physician-in-Chief and Executive Vice President

Thomas Burke, M.D., Executive Vice President, MD Anderson Cancer Network

ACS: Tobacco May Kill More Than Previously Estimated

By Matthew Bin Han Ong

Cigarette smoking may kill tens of thousands more from diseases that are not currently counted as caused by smoking, according to a decade-long study led by American Cancer Society researchers.

Published in the New England Journal of Medicine, the new study included data from nearly a million U.S. men and women age 55 or older that enrolled in five U.S. cohort studies—the American Cancer Society's Cancer Prevention Study-II, the Nurses' Health Study, the Health Professionals Follow-up Study, the Women's Health Initiative, and the National Institutes of Health-AARP Diet and Health Study.

During the approximately 10 years the cohorts were followed, there were over 180,000 deaths: researchers found current smokers, as expected, had death rates nearly three times higher than "never smokers." The study used 95 percent confidence intervals, which were estimated with the use of Cox-proportional-hazards models adjusted for age, race, educational level, daily alcohol consumption, and cohort.

The majority of excess deaths in smokers were due to diseases that are established as being caused by smoking, including 12 types of cancer, coronary heart disease and stroke, and chronic obstructive pulmonary disease.

However, investigators found that about 17 percent of the excess deaths in smokers were due to diseases that have not yet been officially established by the U.S. surgeon general as caused by smoking, and so are not counted in estimates of the death toll from smoking. The surgeon general estimates that each year, smoking

kills about 480,000 Americans.

In particular, smoking was associated with at least a doubling of risk of death from several causes, including renal failure, intestinal ischemia, hypertensive heart disease, infections, and various respiratory diseases other than COPD. Excess risk of death from each of these diseases declined after quitting smoking. The study authors noted that there is strong evidence that smoking is a cause of death from these five diseases, even though they are not currently included in estimates of deaths caused by smoking.

Smoking was also linked with smaller increases in risk of death from other causes not formally established as caused by smoking, including breast cancer, prostate cancer, and cancers of unknown site.

The authors conclude that a substantial portion of excess mortality among smokers may be due to diseases not formally established as caused by smoking, and that, if supported by future research, some of these diseases should be included in future estimates of the death toll from smoking.

"The number of additional deaths potentially linked to cigarette smoking is substantial," said Eric Jacobs, co-author of the study. "In our study, many excess deaths among smokers were from disease categories that are not currently established as caused by smoking, and we believe there is strong evidence that many of these deaths may have been caused by smoking.

"If the same is true nationwide, then cigarette smoking may be killing about 60,000 more Americans each year than previously estimated, a number greater than the total number who die each year of influenza or liver disease."

CMS Announces New Model For Payment & Care Delivery

By Paul Goldberg

The Centers for Medicare and Medicaid Services announced the "Oncology Care Model," a multi-payer payment and care delivery model to support care coordination of cancer care.

The initiative will be focused on three areas:

• Linking payment to quality of care,

• Improving and innovating in care delivery, and

• Sharing information more broadly to providers, consumers, and others to support better decisions.

According to HHS, the Oncology Care Model relies on episode-based, performance-based payments that financially incentivize high-quality, coordinated care. Participating practices will also receive monthly care management payments for each Medicare fee-for-service beneficiary during an episode to support oncology practice transformation, including the provision of comprehensive, coordinated patient care.

"Based on feedback from the medical, consumer and business communities, we are launching this new model of care to support clinicians' work with their patients," said Patrick Conway, CMS chief medical officer and deputy administrator for innovation and quality. "We aim to provide Medicare beneficiaries struggling with cancer with high-quality care around the clock and to reward doctors for the value, not volume, of care they provide. Improving the way we pay providers and deliver care to patients will result in healthier people."

The Oncology Care Model is a part of the

HHS "better care, smarter spending, healthier people" approach to payment and care delivery models developed by the CMS Innovation Center and advanced by the Affordable Care Act.

"While CMS is to be commended for seeking new approaches to payment, we are disappointed they have chosen to pursue only one model—and one that continues to rely on a broken fee-for-service system," said Richard Schilsky, chief medical officer of the American Society of Clinical Oncology.

In comments submitted to CMS on a draft version of its model, ASCO supported testing OCM as well as other payment reform models to determine new approaches to payment for oncology care. Moreover, ASCO urged the center to test models that include more fundamental reform that moves away from the fee-for-service system.

"ASCO looks forward to working with both public and private payers to explore new payment strategies that better reflect modern oncology practice and support high value, patient-centered care," Schilsky said in a statement.

ASCO said it has developed a comprehensive proposal that matches payments to the work performed by cancer care providers. In May 2014, the Society released Consolidated Payments for Oncology: Payment Reform to Support Patient-Centered Care for Cancer—a detailed proposal for a new approach to physician payment for cancer care services under Medicare—which ASCO has shared with CMS and private insurance companies.

ASCO said it's piloting its proposal in different oncology settings across the country.

The Community Oncology Alliance characterized the CMS model as a step in the right direction.

"The model proposed is generally consistent with COA's Oncology Medical Home payment model, although there are some questions and concerns that we need to address with CMMI, which has been very open to input. Community oncology practices have been on the forefront of implementing novel payment reform pilots with private payers," said Ted Okon, COA executive director. "It's good now to see progress on the Medicare front.

"For too long we have been fighting the detrimental consolidation of physician-directed cancer clinics into large hospital systems causing chemotherapy and other cancer treatments to be more expensive for patients and payers, including Medicare."

According to CMS documents released Feb. 12, OCM will target beneficiaries receiving chemotherapy treatment and the spectrum of care provided to a patient during a six-month episode following the start of chemotherapy.

The agency's document states:

Physician practices that furnish chemotherapy treatment may participate in OCM. In addition, in order to participate in OCM, practices must:

• Provide the core functions of patient navigation;

• Document a care plan that contains the 13 components in the Institute of Medicine Care Management Plan outlined in the Institute of Medicine report, "Delivering High-Quality Cancer Care: Charting a New Course for a System in Crisis";

• Provide 24 hours a day, 7 days a week patient access to an appropriate clinician who has real-time access to practice's medical records;

• Treat patients with therapies consistent with nationally recognized clinical guidelines;

• Use data to drive continuous quality improvement; and

• Use an ONC-certified electronic health record and attest to Stage 2 of meaningful use by the end of the third model performance year.

CMS will track participant performance on a number of quality measures and will provide continual feedback to practices throughout the model. In addition, quality measures will be used to determine the performance-based payments.

OCM is multi-payer model that includes Medicare fee-for-service and other payers such as commercial insurance plans or State Medicaid agencies working together to transform care for all patients living with cancer. CMS invites other payers to participate in OCM by entering into a Memorandum of Understanding with CMS. There may be differences between OCM-FFS and other payers in certain areas, such as selection of quality measures for performance-based payment. However, the approach to practice transformation will be consistent across OCM.

OCM-FFS will use a two-part payment approach for participating oncology practices, creating incentives to improve the quality of care and furnish enhanced services for beneficiaries undergoing chemotherapy treatment for a cancer diagnosis. These two forms of payment include: 1) a monthly $160 per-beneficiary care management payment for Medicare FFS beneficiaries; 2) a performance-based payment for OCM episodes. The per-beneficiary-per-month (PBPM) payment for enhanced services will offer participating practices

financial resources to aid in effectively managing and coordinating care for Medicare FFS beneficiaries. The potential for a performance-based payment will incentivize participating practices to improve care for beneficiaries and lower the total cost of care over the 6-month episode period. The performance-based payment will be determined based on the practice's achievement and improvement on quality measures listed in the Request for Applications. Participants will receive regular Medicare FFS payments during the model. Performance-based payments will be calculated retrospectively following the completion of a 6-month episode.

OCM will cover nearly all cancer types. Episodes will begin on the date of an initial chemotherapy administration claim or an initial Part D chemotherapy claim and will not include services provided prior to that date. OCM-FFS episodes will include all Medicare A and B services that FFS beneficiaries receive during the episode period; certain Part D expenditures will also be included. Episodes will terminate six months after a beneficiary's chemotherapy initiation. The PBPM payment will be discontinued for beneficiaries who enter hospice care. Beneficiaries who receive chemotherapy after the end of an episode will begin a new 6-month episode.

Physician group practices and solo practitioners that provide chemotherapy for cancer and are currently enrolled in Medicare may apply to participate. Other payers, including commercial insurers, Medicare Advantage plans, state programs, and Medicaid managed care plans, are also encouraged to apply. To be considered, interested payers must submit a letter of intent through the Oncology Care Model inbox at OncologyCareModel@cms.hhs.gov by 5:00 p.m., EDT on March 19, 2015.

Interested practices must submit letters of intent by 5:00 p.m., EDT on April 23, 2015. Payers and practices that submit a timely letter of intent will be sent an authenticated web link and password with which to submit an electronic application. Applications must be submitted by 5:00 p.m., EDT on June 18, 2015.

BRCA Testing Rates Jump After Angelina Jolie Story

BRCA gene testing rates increased by nearly 40 percent in the week of Angelina Jolie's 2013 announcement that she carried the BRCA 1 gene mutation and had an elective double mastectomy, according to a new AARP Public Policy Institute study released Feb. 11.

This is the first report quantifying an increase in BRCA testing rates among women enrolled in a large U.S. health insurance carrier.

BRCA testing helps identify treatment options for women with the gene mutations before or after they are diagnosed with breast and/or ovarian cancer, according to NCI.

Prior to Jolie's announcement, women with a cancer diagnosis had more BRCA tests than women who did not, the AARP study found. However, during the week of her public announcement, the increase in BRCA testing among women who did not have a cancer diagnosis was nearly twice that of women with a cancer diagnosis.

The testing rates increased from an average of 350 tests per week to an average of 500 tests per week.

"Our study showed that the BRCA testing rate increased about 40 percent and stayed at an elevated level for the rest of the year after Angelina Jolie's announcement," said AARP Executive Vice President for Policy Debra Whitman.

On May 14, 2013, Jolie announced in The New York Times that she tested positive for the BRCA 1 gene mutation and underwent a preventive double mastectomy to reduce her risk of developing breast cancer. Jolie's story gained immediate and widespread international media attention.

Hereditary genetic defects likely cause about 5 to 10 percent of breast cancers, according to the American Cancer Society. BRCA1 and BRCA2 gene mutations are the most common cause of hereditary breast cancer. Women with either mutation have a high lifetime risk of developing breast and ovarian cancer.

To better understand the so-called "Angelina Jolie effect," AARP, in collaboration with Optum Labs, compared BRCA testing rates based on claims among commercially insured women ages 35 and older in the U.S., before and after Jolie's story was published in 2013.

AARP's Public Policy Institute examined the number and rates of BRCA tests among women covered by a large, national U.S. health insurance carrier before and after Angelina Jolie's May 2013

announcement (January-December 2013). Using data from the Optum Labs database of retrospective administrative claims data, the report also analyzed the age, race/ethnicity, and cancer diagnosis status of women ages 35 and older who received the tests.

BRCA testing rates increased for women among all racial and ethnic groups: 43 percent among white women; 43 percent among Hispanic women; 23 percent among black women; and 16 percent among Asian women.

Women ages 50-64 had the highest BRCA testing rate increase (44 percent), followed by women ages 35-49 (40 percent).

In Brief

Deisseroth Awarded Lurie Prize For Cell and Tissue Imaging

KARL DEISSEROTH was awarded the **Lurie Prize in Biomedical Sciences** for the development of tools to image the functions of cells, especially neurons.

Deisseroth is being recognized by the Foundation for the NIH for leading the development of optogenetics, a technology for controlling cells with light to determine function, as well as for CLARITY, a method for transforming intact organs into transparent polymer gels to allow visualization of biological structures with high resolution and detail. The prize will be presented to Deisseroth May 20 in Washington, D.C.

Deisseroth is the D.H. Chen Professor of Bioengineering and of Psychiatry and Behavioral Sciences at Stanford University and a Howard Hughes Medical Institute Investigator. He first pioneered the field of optogenetics, which has greatly expanded our understanding of normal behavior as well as of diseases like Parkinson's, schizophrenia and depression, by combining genetic manipulation and optics to activate or deactivate precisely targeted brain cells.

His team also pioneered CLARITY, a chemical engineering method for making biological tissues such as the intact brain fully transparent and accessible, and which has already enabled scientists to observe intricate molecular-resolution details within healthy brains as well as brains from Alzheimer's disease and autism patients.

"We are delighted to bestow the Lurie Prize to Dr. Deisseroth for his revolutionary work studying the complex circuitry and function of the brain," said Maria Freire, president and executive director of the FNIH. "Today's outstanding biomedical advances, such as optogenetics and CLARITY, will make their way into standard laboratory practice and ultimately help to alleviate human suffering."

A member of the National Academy of Sciences and the Institute of Medicine, Deisseroth is a practicing psychiatrist. His work is supported by grants from NIH, the Defense Advanced Research Projects Agency, the National Science Foundation, and the Howard Hughes Medical Institute, and he is a working group member for the NIH BRAIN Initiative, a program announced by President Obama to deepen science's understanding of the human brain.

DOUGLAS LOWY received the second annual **Harrington Prize for Innovation in Medicine** from the Harrington Discovery Institute and the American Society for Clinical Investigation.

Lowy is deputy director of the NCI and chief of the institute's Laboratory of Cellular Oncology.

The Harrington Prize was established in 2014 by the Harrington Discovery Institute at University Hospitals and the American Society for Clinical Investigation.

Lowy is being recognized for his key discoveries that led to development of the human papillomavirus vaccine. The vaccine developed by Lowy, in collaboration with Merck and GlaxoSmithKline, and approved by the FDA in 2006, was the first licensed vaccine to prevent cancer by guarding against the sexually transmitted infection that causes the disease.

"I can't think of anyone more deserving than Doug Lowy to receive The Harrington Prize for Innovation in Medicine," said Francis Collins, director of NIH. "Through his leadership in the development of the HPV vaccine, Doug has made profound contributions to the prevention of cervical cancer. He continues to seek ways to reduce the burden of this disease in developing countries."

"Dr. Lowy is an exemplary physician-scientist. His research with former trainee John Schiller helped to identify key aspects of the biology of HPV that guided development and ultimately FDA approval for a vaccine that has significantly improved human health globally," said Mukesh Jain, scientific director of the Harrington Discovery Institute and current president of the ASCI.

In addition to receiving a $20,000 honorarium, Dr. Lowy will deliver the Harrington Prize Lecture at the 2015 ASCI and Association of American Physicians Joint Meeting on April 24, and publish a review in the April issue of the Journal of Clinical Investigation.

He is an elected member of the National Academy of Sciences and is recipient of numerous awards and honors including the National Medal of Technology and Innovation.

UT SOUTHWESTERN and a Texas consortium plans to establish the country's first **National Center for Heavy Ion Radiation Therapy**, targeted for completion in 2021. NCI awarded UT Southwestern a $1 million planning grant to develop research proposals for the center.

The consortium consists of researchers from UT Southwestern, MD Anderson Cancer Center, Texas A&M University, Prairie View A&M University, Baylor College of Medicine, The UT Health Science Center at San Antonio, The UT Medical Branch at Galveston, and NASA, in addition to national and international collaborators. Hak Choy, chair and professor of Radiation Oncology at UT Southwestern, is principal investigator for the award.

Eight operational heavy ion radiation therapy centers exist in Japan, Germany, Italy and China. Ten additional centers are in development, according to UT Southwestern.

Building costs for the center are estimated at $200 million to $250 million, and would need a combination of federal, state, and private funding for construction and ongoing research.

WENDY SELIG plans to step down as president and CEO of the **Melanoma Research Alliance**, posts she has held for the past five years, in order to establish a new consulting venture.

Debra Black, a founder and chair of MRA, expressed her and the board's appreciation for the contributions Ms. Selig has made during the time she headed MRA.

"Wendy importantly helped oversee and develop the growth of MRA almost from the start into its becoming the leading private funder of melanoma research worldwide with more than $60 million in cutting edge research grants across 14 countries. We are greatly appreciative and wish Wendy the best of luck in her new endeavor," said Black.

Selig will continue an association with MRA as a consultant, said Black. A search for her replacement is currently underway.

THE MULTIPLE MYELOMA RESEARCH FOUNDATION and **Inflection Biosciences** announced a collaboration to test IBL-202, a dual-kinase inhibitor, in the treatment of myeloma.

Investigators will test the effectiveness of IBL-202 alone and in combination with other therapeutics in preclinical models of multiple myeloma. IBL-202 inhibits both the PIM and PI3K regulators.

This collaboration will be conducted through MMRF's Translational Network of Excellence program, which supports early-stage research and evaluating drugs in the preclinical setting.

NORTHWESTERN UNIVERSITY's Robert H. Lurie Comprehensive Cancer Center, in collaboration with the Northwestern Medicine Developmental Therapeutics Institute and Northwestern Memorial Hospital, has launched a new research program, **Northwestern Onco-SET**, to provide a personalized, precision medicine option.

The program will initially focus on patients with any type of cancer that is not responsive to traditional therapies. Onco-SET plans to sequence individual genetic profiles of tumors and provide site-agnostic, pathway-driven treatments.

Onco-SET created the Lurie Cancer Center's Molecular Tumor Board, which will review every tumor's genomic profile. The board is comprised of cancer specialists including pathologists, medical, surgical and radiation oncologists, cancer geneticists, genome biologists, molecular scientists, bio-ethicists and bioinformaticists. Treatment options made available to the Molecular Tumor Board through Onco-SET include novel therapies from a variety of early-stage clinical trials.

Drugs and Targets

E.U. Expands Velcade Label; ODAC to Examine Talimogene Laherparepvec in Melanoma

The European Commission approved a variation to the terms of the marketing authorization of **Velcade (bortezomib)**, in combination with rituximab, cyclophosphamide, doxorubicin and prednisone, for the treatment of adult patients with previously untreated mantle cell lymphoma who are unsuitable for blood stem-cell transplantation.

The decision follows a positive opinion from the Committee for Medicinal Products for Human Use of the European Medicines Agency on Dec. 18, 2014. This approval allows for the marketing of Velcade for the above indication in all 28 countries of the European Union. The approval of Velcade in MCL is based on data from the phase III LYM-3002 study.

In the E.U., Velcade is currently indicated for the treatment of multiple myeloma either as monotherapy or in combination with other treatment regimens.

LYM-3002 was a randomized, open-label,

prospective phase III study including 487 patients with newly diagnosed MCL who were ineligible or not considered for bone marrow transplantation.

The study compared patients with MCL using the Velcade-based combination, compared to a standard of care combination of rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone. The Velcade combination significantly improved progression-free survival, the primary endpoint.

An independent review committee reported the increase in PFS to be 59 percent (median 24.7 vs. 14.4 months; HR 0.63; $p<0.001$), whereas the study investigators reported the increase in PFS to be 96 percent (median 30.7 vs. 16.1 months; HR 0.51; $p<0.001$).

In 2006, the FDA approved Velcade for the treatment of patients with MCL who have received at least one prior therapy, with a subsequent frontline treatment approval in October 2014 for Velcade in combination with rituximab, cyclophosphamide, doxorubicin, and prednisone.

The FDA Oncologic Drugs Advisory Committee and the Cellular, Tissue and Gene Therapies Advisory Committee will jointly review **talimogene laherparepvec** for the treatment of patients with injectable regionally or distantly metastatic melanoma at a meeting April 29.

The Prescription Drug User Fee Act action date for completion of FDA review of the talimogene laherparepvec, sponsored by Amgen, is Oct. 27.

CTGTAC is utilized by the FDA to review and evaluate data relating to the safety, effectiveness and appropriate use of human cells, human tissues, gene transfer therapies and xenotransplantation products. ODAC reviews and evaluates data concerning the safety and effectiveness of marketed and investigational human drug products for use in the treatment of cancer and makes recommendations to the FDA.

Talimogene laherparepvec is an investigational oncolytic immunotherapy designed to selectively replicate in tumors, but not normal tissue, and to initiate an immune response to target cancer cells that have metastasized.

Merck and Bristol-Myers Squibb have agreed to transfer full responsibility for the promotion of Erbitux (cetuximab) to Merck in Japan as of May 1.

Erbitux was launched in collaboration with Bristol-Myers Squibb in Japan in September 2008 for the treatment of metastatic colorectal cancer, followed by an additional indication for the treatment of head and neck cancer, approved in December 2012.

Merck licensed the right to market Erbitux outside the U.S. and Canada from ImClone LLC, a wholly-owned subsidiary of Eli Lilly and Company, in 1998. Erbitux has obtained market authorization in over 90 countries for the treatment of colorectal cancer and for the treatment of squamous cell carcinoma of the head and neck.

FDA granted Orphan Drug Designation to Reolysin, developed by Oncolytics Biotech Inc., for the treatment of ovarian cancer.

Oncolytics has supported two sponsored clinical studies assessing Reolysin in the treatment of ovarian cancer. The first was a phase I/II clinical trial for patients with metastatic ovarian, peritoneal and fallopian tube cancers using concurrent intravenous and intraperitoneal administration of Reolysin that provided evidence of viral targeting and replication in peritoneal and ovarian cancer cells. The second is an ongoing randomized phase II trial of weekly paclitaxel versus weekly paclitaxel with Reolysin in patients with persistent or recurrent ovarian, fallopian tube or primary peritoneal cancer, which completed enrollment in September 2014.

Roche acquired **Signature Diagnostics AG**, a privately held company based in Potsdam, Germany, that develops large blood plasma and tissue biobanks in multiple cancers, including colorectal and lung, which are constructed from multicenter prospective clinical studies.

Signature uses the samples from its biobanks along with accompanying clinical progression and genetic data to develop and validate circulating cell free DNA tests which have the potential to advance non-invasive treatment response monitoring for patients with cancer.

Signature will be integrated into Roche Sequencing Unit and will continue to focus on expanding its genomic signature portfolio.