THE CANCER LETTER

Jan. 30, 2015 • www.cancerletter.com • Vol. 41 No. 4

Charles Blanke at Horsethief Butte, Wash.

Guest Editorial

SWOG Chair Blanke to Climb Mt. Kilimanjaro To Draw Attention to Clinical Trials Funding

By Charles D. Blanke

Rising 19,341 feet above sea level, Mt. Kilimanjaro is the highest mountain in Africa and the tallest freestanding mountain in the world. It is a dormant but non-extinct volcano which last erupted some 150,000 years ago.

Next week I will climb Mt. Kilimanjaro to draw attention to the risks posed by financial cuts to publicly funded cancer clinical studies, to raise funds to help fill the gaps those cuts have left, and to pay homage to some 200,000 SWOG trial volunteers.

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Draft Bill Seeks to Revamp FDA, NIH, CMS To Accommodate 21st Century Science

By Paul Goldberg

The House Committee on Energy and Commerce Jan. 27 released a draft version of a massive bill that seeks to streamline the pathways of innovation in medicine.

The 393-page "discussion document," which sets forth the committee's long-awaited 21st Century Cures initiatives, includes proposals reworking many important structures in funding medical research and the regulatory

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In Brief

Strong Named Chief of GI Surgery Division At Northwestern Memorial Hospital

SCOTT STRONG was named as chief of the Division of Gastrointestinal and Oncologic Surgery at **Northwestern Memorial Hospital** and surgical director of the Digestive Health Center.

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Blanke to Climb Kilimanjaro To Raise Money for Research

(Continued from page 1)

Clinical oncology has made immense progress over the past half-century, in terms of our ability to extend and improve the lives of patients with cancer. The NCI cooperative groups, now called Network groups, have consistently contributed to that progress, through the design and conduct of carefully thought-out clinical trials.

Indeed, a huge percentage of the oncologic treatments patients receive today first proved their safety and effectiveness via formal clinical study. Thousands of these trials, particularly those not suited for even large academic cancer centers, or pharmaceutical companies, have been conducted by this extraordinary cooperative group network, with its tens of thousands of researchers, at institutions worldwide.

Readers of The Cancer Letter know we are poised to potentially make huge breakthroughs in effective treatments for a variety of malignancies, through our increasing knowledge of genetics and cancer immunology. Ironically, a decline in federal funding for the NCI's clinical trials system has significantly slowed the pace of our progress.

This funding decline has been well chronicled, in these pages and others, as have its results: We conduct fewer trials. We will enroll fewer patients. As a result, we support the work of fewer gifted young researchers.

I have been an avid rock climber and amateur mountaineer for thirty years, and I have always wanted to reach one of the Seven Summits (the highest mountaintop on each of the Earth's continents). An expedition to Kilimanjaro, sponsored by an alpine organization I am a life member of—the Mazamas—seemed like the perfect vehicle to meet a number of my, and SWOG's, goals.

In early February, I will be joining the Mazamas' Kilimanjaro expedition to raise awareness of the risks posed by financial cuts and, with something akin to a 10K run (except it's a 45 mile, ~20,000 foot high run) or an ice bucket challenge, I am also fund raising. Specifically, with the support of the Alliance, the Childrens' Oncology Group, and ASCO's Conquer Cancer Foundation, I'm soliciting donations to help offset those federal cuts.

We have already raised over $100,000 in donations, with an ultimate goal of $250,000. It's not nearly enough to bridge this past year's funding gap, but it may serve as the basis for some new grants, or allow some interesting correlative components to future clinical trials. I am happy to report virtually all of the monies raised (98%) will go to support cancer research.

I have two other goals for the climb.

We have already received some very nice TV and print coverage, hopefully helping us achieve our goal to increase the public's awareness of the deficit, and the underlying importance of clinical oncology research in general.

Also, since our founding in 1956, SWOG has led more than 1,000 studies and has enrolled more than 200,000 volunteers on our trials. I particularly want to note the contributions of these 200,000. These trial volunteers are heroes who have contributed so much, and placed so much trust in us, their oncologists. In large part, I'm making the climb to honor them.

The best way I know to do that is to bring wider public attention to what they have offered, to the astonishing benefits they've brought to patients who followed them, and to the need for more cancer patients and healthy volunteers alike to join clinical trials.

I will be taking almost 200,000 of those clinical trial volunteers mentioned above with me up Kilimanjaro, their initials emblazoned on a large banner we will unfurl at the summit.

I'll be partnering on the climb with fellow SWOG oncologist Brett Sheppard.

Though I've climbed mountains throughout the Northwest for many years, Kilimanjaro takes the challenge to a whole new level.

To acclimate my body to the lower oxygen levels near Kilimanjaro's summit, I have been using a normobaric, high-altitude sleeping tent nightly for the past several weeks. I've also been engaged in a rigorous physical conditioning program with several

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Editorial, Subscriptions and Customer Service:
202-362-1809 Fax: 202-379-1787
PO Box 9905, Washington DC 20016
General Information: www.cancerletter.com

Subscription $405 per year worldwide. ISSN 0096-3917. Published 46 times a year by The Cancer Letter Inc.

of my co-climbers. Having Type 1 diabetes brings me some unexpected mountain-climbing challenges, such as how to keep my insulin from freezing at high altitude.

I'll be blogging throughout my climb, with postings to http://www.facebook.com/ClimbforCancerClinicalTrials, and will be using a tracking app that will report my location every few minutes. Those who are curious can watch our progress in real time at http://www.swog.org/Kilimanjaro.

The American Cancer Society reported last month that 1.5 million cancer deaths were avoided in the United States over the last two decades due to improvements in treatment and prevention. The investment and sacrifices made by the 200,000 we will be honoring on Mt. Kilimanjaro, and by hundreds of thousands of others like them, have brought us to this critical point. We must repay them by re-committing to public support for the cancer clinical research they gave themselves to so fully.

The author is the chair of SWOG and professor of medicine at the Knight Cancer Institute at the Oregon Health and Science University.

21st Century Cures Bill Proposes Change at NIH, FDA, CMS & CDC

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approval processes—from strengthening the authority of the NIH director and boosting the size of the NIH Common Fund, to including new incentives for makers of orphan and generic drugs to changing the manner in which FDA reviews drugs and devices.

According to Rep. Fred Upton (R-Mich.), the committee chair, the just-released draft is a kitchen sink of ideas. The committee said it's seeking feedback on the proposals that made it into the document, with the goal to introduce legislation and send a bill to President Obama by the end of 2015.

The logo of the 21st Century Cures initiative—Discovery → Development → Delivery—echoes the promises often repeated by former NCI Director Andrew von Eschenbach, whose goal at the institute was to eliminate suffering and death due to cancer by the year 2015. Von Eschenbach reorganized NCI around the "3 Ds" (The Cancer Letter, May 19, 2006). Von Eschenbach now focuses on FDA reform at the Manhattan Institute, a conservative think tank.

"The document is a starting point in the legislative process to spur discussion," the Committee on Energy and Commerce said in a statement. "The inclusion of a policy in this draft should not be seen as an endorsement. Some ideas may be added while other ideas may be dropped as the discussion moves forward, creating an improved final product shaped by this open and transparent process."

The draft is being produced after eight hearings, 19 round table discussions and five white papers. Though the bill's sponsors said their goal is to stay bipartisan, Democrats are stopping short of endorsing this initial version of the legislation.

"Throughout this initiative, we have done things differently," Upton said in a statement. "We have been bipartisan from the get-go, we spent a year listening and asking questions, and we have been fully transparent at every step. Transparency and collaboration have been and will continue to be the hallmarks that drive our success. These ideas represent an important milestone—a critical first step in a legislative process.

"Our solutions to boost cures and jobs are starting to take shape as we move from broad principles to legislative language. However, this document is far from the final product. Some things may be dropped, some items may be added, but everything is on the table as we hope to trigger a thoughtful discussion toward a more polished product."

Rep. Diana DeGette (D-Colo.), who is leading the initiative on the Democratic side, praised the initial version of the bill, without fully endorsing it.

"From the beginning of the 21st Century Cures initiative, Chairman Upton and I have paid special attention to public engagement, idea-sharing, and feedback," DeGette said. "In that vein, I appreciate his effort today to publicly share possible legislative language on a number of proposals that might be included in an eventual bill. As Chairman Upton and I begin to draft the bill itself, we look forward to receiving feedback on the issues identified in his draft document and other suggestions. While I don't endorse the draft document, I know that with continued engagement, we can reach a bipartisan consensus to help advance biomedical research and cures."

Insiders say that Democrats are waiting for political horse-trading to begin.

Broad as it is, the document also includes "placeholders," promises that an even broader array of issues could be included.

Several Capitol Hill insiders said they are asking their groups to focus on a manageable number of areas—three or four at the most—as the bill moves forward.

"We are very excited about the promise of this bill," said Ellen Sigal, chair and founder of Friends of

Cancer Research. "It's early, and we have to see all the moving parts of it, but we are very exciting that people are working together toward the goal that will actually help patients."

FOCR played a key role in developing the concepts around three sections of the bill that address three cancer-related issues.

According to a FOCR summary, these areas are:

1. Development and Use of Patient Experience Data

Problem: Current drug research and development processes are based on historically acceptable endpoints and rarely incorporate information about the patient's experience with the disease.

Solution: In order to build on the Patient Focused Drug Development meetings established in FDASIA, a series of new steps could operationalize the incorporation of direct patient feedback and assist patient advocacy organizations, medical researchers, FDA, and industry to realign drug development. Putting the patient experience at the start of the development can help ensure that the aspects of diseases that patients determine are the most important to treat are addressed and transform the way in which new treatments are evaluated.

Additional background information is available here.

2. Streamlining Supplemental New Drug Applications

Problem: Supplemental new drug applications (sNDA) are submitted to the FDA with evidence to support the safe and effective use of a drug in a treatment setting different than the original approval. Because a great deal is understood about these drugs from prior uses, treating new and supplemental drug applications identically may be an inefficient use of limited time and resources.

Solution: In 2013, FDA received 134 sNDA/sBLA efficacy supplements, which require a significant amount of time and effort to review. Other regulatory bodies around the world utilize summary information of trial results to make approval and labeling decisions. A similar approach in the US could allow better allocation of resources for FDA personnel and result in shorter sNDA review periods for drug sponsors. A pilot program would be established for drugs with >3 prior indications on their label to which sponsors could voluntarily apply. This could encourage greater utilization of the sNDA process if sponsors knew that they could get their product on the market faster.

Additional background here.

3. FDA Hiring & Retention Processes

Problem: Continually increasing FDA responsibilities has caused other routine functions of the agency to suffer, such as continuing education and travel for FDA staff, and adversely impacted FDA's ability to recruit and retain senior scientific and executive positions. Hiring new employees can be onerous and time consuming to the point that it extremely difficult to address agency priorities as they emerge.

Solution: Enabling FDA to greater utilize direct hiring mechanisms and pay scale enhancements for mission critical positions would allow for expedited procedures and to attract top talent within timeframes and at compensation levels comparable to other sectors.

A Bird's Eye View of Gargantuan Document

The massive discussion document describing the Congressional 21st Century Cures initiative is a massive amalgamation of original legislative proposals, pending bills and placeholders.

In the full document, which is posted here, the proposals are grouped into five sections:

TITLE I—*Incorporating Patient-Reported Outcomes into Regulatory Process*

A series of proposals on patient-focused drug development, biomarker qualification, antibiotic drug development, dormant therapies, and device review pathways.

• FDA would be required to establish a structured framework for the meaningful incorporation of patient experience data into the regulatory decision-making process, including the assessment of desired benefits and tolerable risks associated with new treatments.

• FDA would be mandated to establish a process for consideration, and possible qualification, of surrogate endpoints. The provision also would allow FDA to use private-public partnerships to qualify other types of biomarkers.

• FDA would would be allowed to approve a drug that has received a breakthrough therapy designation when early stage clinical data provides sufficient evidence under the current safety and efficacy standards, considering the risks and benefits of the drug and the risks associated with the

disease or condition for which unmet medical needs exist.

• FDA would have the option to conduct expedited review of devices that represent breakthrough technologies with the potential to address unmet medical needs. Also, an accelerated approval process would established.

• Transparency requirements would be placed on drug companies regarding their expanded access programs. An expanded access task force to provide recommendations to Congress for further reforms of the program would be formed.

• Review process supplemental indications would be streamlined by allowing FDA to accept and review data summaries rather than full data packages.

• The Dormant Therapies Act would seek to foster investment in treatments and cures for patients where there are unmet medical needs. It would allow innovators to choose a new pathway and receive a fixed year protection period for these therapies upon FDA approval. This change would shift research and development towards therapies based on scientific promise and patient need, rather than patent life. It also would reward investment in treatments and cures for complex diseases where it takes longer to develop safe and effective therapeutics.

• Six months of additional market exclusivity for a drug if the sponsor establishes that the drug treats a rare disease and receives a rare disease indication from FDA on its label.

TITLE II—*Enhancing Science, Including Helping Young Scientists*

Proposals to help aid in the discovery, development, and delivery of the next generation of patient-centered solutions by establishing the 21st Century Cures Consortium, fostering innovation in health information technologies through the SOFTWARE Act, and helping young scientists.

• A Medical Product Innovation Advisory Commission would be created to advise Congress on issues related to the discovery-development-delivery cycle. The commission would be based on MedPAC.

• FDA would be required to update its guidance on surrogate and intermediate endpoints for the accelerated approval of regenerative medicine products.

• This includes language from the recently released discussion draft based on H.R. 3303, the SOFTWARE Act, which seeks to provide a regulatory framework for developing apps and health information technologies.

• Creating a data sharing framework to enable (1) patients and physicians to better identify ongoing clinical trials, thereby increasing opportunities for patients in need of a treatment, (2) researchers and developers to use Medicare data for the purposes of improving the quality of patient care, and (3) a process for Congress to address other issues identified by the President's Council of Advisors on Science and Technology.

• Authorizing FDA to utilize real world evidence and require FDA to issue guidance on collecting such evidence.

• Addressing the process of coverage with evidence development.

• FDA would be required to set forth additional guidance on the review process for products that include both drugs and devices.

• A requirement that recipients of NIH grants share their data, subject to confidentiality and trade secret protections.

• A provision would open the data siloed in health care facilities in order to enable patients who want to play a more proactive role in finding better treatments or a cure for their disease to do so in a responsible manner that continues to protect their privacy.

• Establish a program at NIH to help young emerging scientists.

• Require NIH to support projects that pursue innovative approaches to major challenges in biomedical research that are high-risk, but have the potential to lead to breakthroughs.

TITLE III—*Modernizing Clinical Trials*

By reducing regulatory overlap and administrative inefficiency, in addition to encouraging broader utilization of efficient, flexible trial designs, provisions in Title III seeks to modernize the development and assessment of potential new treatments and keep clinical trials from moving overseas by improving the cost and speed of trials.

• Streamline the institutional review board process, particularly for clinical trials conducted at multiple sites, by minimizing regulatory duplication and unnecessary delays.

• Encourage the broader application of Bayesian statistics and adaptive trial designs.

• Ensure that FDA and sponsors periodically evaluate whether post-approval studies remain scientifically warranted.

• Require NIH to implement the National Pediatric Research Network Act, which was established as part

of the PREEMIE Reauthorization Act (P.L. 113-55).

• Set forth a Sense of Congress that NIH and FDA should work with European Union, industry, and others to establish a global pediatric clinical trial network.

TITLE IV—*Accelerating Discovery, Development and Delivery at NIH, FDA, CDC, and CMS*

A series of proposals intended to streamline regulatory processes and equip our federal public health agencies with the tools needed to ensure they are able to keep pace with innovation.

• NIH would be required to issue a strategic plan.

• Biomedical research working group composed of NIH and stakeholders would be established to provide recommendations on how to streamline the grant process for researchers.

• NIH director would be given greater authority over the institutes and centers at NIH.

• Additional funding would be given to the NIH Common Fund.

TITLE V—*Modernizing Medical Product Regulation*

Policies developed to encourage modern manufacturing technologies here in the United States as well as provisions intended to update certain medical device regulations.

• Additional incentives would be provided for manufacturing generic drugs here in the U.S.

• FDA would be required to update its guidance regarding novel manufacturing techniques.

• The definition of valid evidence acceptable to FDA would be broadened to

include well-documented, real world evidence gathered from clinical registries and studies published in peer-reviewed journals.

• The advisory committee process would be "streamlined."

• Establishing a national framework for licensure of medical device wholesalers and third-party logistics providers, similar to what Congress enacted for prescription drugs in the Drug Quality and Security Act.

Duke Trial Delayed, But University to Turn Over More Documents

By Paul Goldberg

The trial stemming from Duke University's clinical trials of a fraudulent genomic technology has been delayed, most likely until September.

The attorneys who represent the seven plaintiffs in Aiken vs. Duke initially sought the delay. Struck by the flu, the attorneys, including the lead counsel, were in no condition to deliver opening arguments Jan. 26.

However, even as the principal case has been continued, the judge in Durham County Superior Court Jan. 29 heard an argument over discovery, ordering Duke to turn over additional materials to the plaintiffs.

The argument is about roughly 1,400 internal documents, some of which Duke designated as either privileged or not responsive to the discovery request.

These documents would now be either turned over to the plaintiffs or examined by a special master to determine whether they are indeed covered by attorney-client privilege.

The ruling by Judge Robert Erwin could boost the case against Duke by giving the plaintiffs more ammunition and additional time to further boost the case that was sparked by fraud that has been directly tied to the former Duke faculty star Anil Potti.

However, the controversy is not limited to Potti.

Documents show that Potti's mentor and protector Joseph Nevins, aided by a phalanx of deans, had silenced a whistleblower who spotted problems in the Potti lab (The Cancer Letter, Jan. 9).

These same deans subsequently stated falsely to a committee of the Institute of Medicine that no whistleblower had come forward to warn them about Potti.

An internal email from a Nevins and Potti associate, Holly Dressman, stated that she had doubts about one of the predictors derived by Potti. Dressman also expressed concern about the prospect of NCI statisticians getting hold of the data (The Cancer Letter, Jan. 16).

Though clearly relevant—indeed crucial—for determination of what Duke officials could have been expected to know about Potti's fraud, the Dressman memo wasn't turned over in discovery by Duke officials. In a filing, the plaintiffs said they obtained it from Potti's attorneys as they prepared to depose the disgraced researcher.

Altogether, 117 patients enrolled in Duke's three clinical trials.

Duke officials argued that none of the patients were harmed. Experts in bioethics and misconduct say that

misleading dying patients constitutes harm and further stating that Duke's institutional response to the scandal was flawed (The Cancer Letter, Jan. 23).

According to Triangle Business Journal, the controversy revolves around 1,400 documents. Attorneys for Duke and Potti had access to these documents, but the plaintiffs' side didn't.

"The court has some concern about that because obviously some of these documents have some relevance," Judge Erwin said at the pre-trial hearing Thursday. "The question becomes how to alleviate that heartburn."

"What other data are out there about this fraudulent research?" plaintiffs' attorney Thomas Henson asked, according to the Triangle Business Journal. "Why is that such an unreasonable request."

Ervin said he would work with a special master, likely a retired judge, to release the documents.

Duke's Califf to be No. 2 at FDA

Robert Califf was named FDA Deputy Commissioner for Medical Products and Tobacco, a de facto No. 2 post at the agency.

Califf, 63, an expert in cardiology, clinical research, and medical economics, is leaving his job as vice chancellor of clinical and translational research at Duke University. He will join the agency in late February.

Califf will oversee the FDA Center for Drug Evaluation and Research, the Center for Biologics Evaluation and Research, the Center for Devices and Radiological Health, and the Center for Tobacco Products. He will also oversee the Office of Special Medical Programs in the Office of the Commissioner.

According to an FDA announcement, Califf will provide high-level advice and policy direction on medical product and tobacco priorities and will manage clinical, scientific and regulatory initiatives in several key areas for the agency, including personalized medicine, orphan drugs, pediatric science, and the advisory committee system.

"I am delighted to announce this important addition to FDA's senior leadership team," FDA Commissioner Margaret Hamburg said in a statement. "Dr. Califf's deep knowledge and experience in the areas of medicine and clinical research will enable the agency to capitalize on, and improve upon, the significant advances we've made in medical product development and regulation over the last few years."

Califf will be taking a leave of absence after 33 years at Duke. In a press call Jan. 26, he said he intends to return. At the press call, Califf said he has been interviewed for the job of FDA commissioner twice before, during the Bush and Obama administrations.

Califf has served as director of the Duke Translational Medicine Institute and professor of medicine in the Division of Cardiology. Prior to that, he was the founding director of the Duke Clinical Research Institute, which is described as the world's largest academic research organization.

Califf is recognized by the Institute for Scientific Information as one of the top 10 most cited medical authors, with more than 1,200 peer-reviewed publications.

He was a member of the Institute of Medicine committees that recommended Medicare coverage of clinical trials and the removal of ephedra from the market, and of the IOM's Committee on Identifying and Preventing Medication Errors. In addition, he served as a member of the FDA Cardiorenal Advisory Panel and FDA Science Board's Subcommittee on Science and Technology. Currently, he is a member of the IOM Policy Committee and liaison to the Forum in Drug Discovery, Development, and Translation.

Califf had no oversight authority over clinical trials of genomic predictors that were constructed by Duke scientists Joseph Nevins and Anil Potti. The predictors have since been discredited as fraudulent and publications describing them have been retracted.

High-level academic administrators at Duke were involved in keeping the research and clinical trials going, silencing a whistleblower and ignoring doubts expressed by lab insiders. Califf's name doesn't figure in any of the internal Duke e-mails obtained by The Cancer Letter.

Califf stepped into the scandal at a later date, helping investigate it and acting as a point person in interactions with a panel of the Institute of Medicine and speaking for Duke to the CBS news program 60 Minutes.

During the press call, Califf said his move was unrelated by the Duke genomics scandal.

"If I had wanted to leave because of the Potti case, it would have been a few years ago," he said on the call, as quoted in the Triangle Business Journal.

"I wish I had gotten myself more involved earlier," Califf said at the press call. "There were systems that were not adequate, as we stated...That was a tough one, I think, for the whole institution.

"We learned the importance of high-quality evidence, and not just taking somebody's word for it."

Desequestration?

Obama, Congress Seek to Restore Federal Funding

By Matthew Bin Han Ong

President Barack Obama and several members of Congress announced a slew of initiatives this week aimed at eliminating the effects of sequestration for the government, and for medical research by providing increases for NIH and other federal agencies.

Two bills introduced in Congress would provide sustained increases by boosting funding through direct appropriation and by adjusting caps established in the Budget Control Act.

The American Cures Act, introduced by Sen. Dick Durbin (D-Ill.), would adjust the budget caps to allow for 5 percent annual funding increases over 10 years for NIH, CDC, the Department of Defense Health Program, and the Veterans Medical & Prosthetics Research Program.

The Accelerating Biomedical Research Act, introduced by Rep. Rosa DeLauro (D-Conn.) would boost the NIH budget by 10 percent for the next two years, followed by a 5 percent increase in each following year through 2021.

President Barack Obama called Jan. 29 for a 7 percent hike in spending above the budget caps. The president's 2016 federal budget proposal would include about $74 billion in discretionary spending above sequestration levels.

Obama's new Precision Medicine Initiative, announced in his State of the Union address, receives $215 million in the president's budget proposal, and would pioneer a new model of research that promises to accelerate biomedical discoveries and provide clinicians with new tools, knowledge, and therapies to select which treatments will work best for which patients.

The initiative would provide: $130 million to NIH for development of a voluntary national research cohort, $70 million to NCI to boost genomic research, $10 million to FDA to acquire addition expertise and develop databases, and $5 million to the Office of the National Coordinator for Health Information Technology.

"Cancer costs our economy nearly $216 billion in combined direct and indirect medical costs each year," the American Cancer Society Cancer Action Network said in a statement. "The president's proposal is a smart investment and we call on Congress to make funding for the Precision Medicine Initiative and cancer research broadly a top priority in the FY16 budget."

The initiative's emphasis on genomics is appropriate, said Research!America President and CEO Mary Woolley.

"President Obama's Precision Medicine Initiative could potentially drive medical and health research into exciting, new territory as we advance efforts to develop the right treatments at the right time for individual patients," Woolley said. A laser-focus approach that takes into account a patient's genetic profile, environment and lifestyle is critical to treat diseases such as cancer, which afflicts millions of Americans.

"Only about a quarter of Americans believe the U.S. has the best health care system in the world, according to public opinion polling commissioned by Research!America. This initiative could help reverse both the perception and the reality with targeted treatments that will save lives and improve health care delivery.

"This initiative is an important development for patients, physicians and researchers who will benefit from a stronger national commitment to precision medicine and for those who may yet take advantage of the new tools and therapies that will result from this effort. And many Americans are ready to support this endeavor.

"Polls show more than half say they are willing to share their personal health information to advance research and help improve patient care, and a majority believes that elected officials should listen to advice from scientists. This initiative is a major step towards building a stronger public-private partnership to leverage health data and technology to accelerate the discovery and development of tailored treatments for patients."

Research advocates say Durbin and DeLauro's bills would help to restore NIH's lost purchasing power—precipitated by the decline of regularly appropriated funds for research in recent years.

"The proposal[s] would help to put funding back on track toward levels that would have been maintained if Congress had appropriated funds year over year that kept pace with medical inflation," said Christopher Hansen, president of the ACS CAN.

"We are hopeful that [the bills] will prioritize cancer research and prevention, as more than 1,600

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Americans are still dying from the disease every day. At this critical moment of opportunity, when our understanding of cancer genetics has the potential to be translated into new early detection tests and therapies, robust and sustained funding is critical.

"As the largest public funder of cancer research, the federal government plays a critical role in our ability to eliminate death and suffering from cancer. That investment is further multiplied as private industry leverages basic scientific discovery that translates into lifesaving detection tools and therapies.

"ACS CAN urges Members of Congress to support this important proposal and make the fight against cancer a national priority."

Carrie Wolinetz, president of United for Medical Research, commended the bills.

"With stagnant funding levels surpassing a decade, our nation is falling deeper and deeper into a medical innovation deficit," Wolinetz said. "These steadfast congressional leaders recognize our country's dire position and the importance of making lifesaving and economy-fueling NIH funding a top priority in the 114th Congress.

"In the coming weeks, United for Medical Research, in partnership with the Information Technology & Innovation Foundation, will release a report that explores new approaches to achieving steady funding growth for NIH. As a nation with a rich history of landmark medical discoveries, from mapping the human genome to eliminating the polio epidemic, we urge Congress to restore its commitment to medical research."

In Brief

Strong Named Chief of Division At Northwestern Memorial

(Continued from page 1)

Strong will serve in partnership with Stephen Hanauer, the medical director of the Digestive Health Center, to help develop the center's clinical, research and educational initiatives. In addition, Strong was appointed as the James R. Hines, MD, Professor of Surgery at the Northwestern University Feinberg School of Medicine.

Strong came to Northwestern Medicine from the Cleveland Clinic where he was a surgeon in the Department of Colorectal Surgery since 1992 and won several awards, including the Premier Physician Award from the Crohn's and Colitis Foundation of America's Northeast Ohio Chapter. He also worked internationally with Cleveland Clinic, as the chief medical officer and chief executive officer at Sheikh Khalifa Medical City in Abu Dhabi, United Arab Emirates.

JAMES ORR was appointed chair of the **Florida Board of Medicine**. Orr is medical director of Florida Gynecologic Oncology, a division of 21st Century Oncology. He will direct the actions of the board that oversees 68,000 Florida physicians.

He has served on the board since 2010, and most recently served as the board's vice chair in 2013.

Previously, Orr served as president of the Society of Gynecologic Oncology, the Florida Society of Gynecologic Oncology, and the Florida Obstetrical and Gynecologic Society. He received the Saks Fifth Avenue Humanitarian Award for his compassionate

efforts in Gynecologic Oncology, as well as the "Best Doctors for Women" distinction from Good Housekeeping magazine.

Orr has published more than 120 peer reviewed articles, four textbooks, and 33 chapters to scientific textbooks, as well as served as the Associate Editor of Journal of Gynecologic Oncology and the American Journal of Clinical Oncology.

COLUMBIA UNIVERSITY has eliminated its mesothelioma center after its director, **Robert Taub**, was reported to have had a long-running association with the former New York State Assembly Speaker **Sheldon Silver**.

"Dr. Taub no longer serves as director of the mesothelioma center," said Douglas Levy, a spokesman for Columbia University Medical Center. "Its research and patient care activities of are being absorbed into the Division of Hematology/Oncology." Taub remains on the Columbia faculty, Levy said.

Silver faces federal corruption charges, which include directing New York state grants to Taub, who referred mesothelioma patients to a law firm that employed Silver. Taub was not identified by name in the court documents.

According to federal charges, Silver received more than $5.3 million in payments from the Weitz & Luxenberg law firm. The funds came in the form of: "(i) a salary of approximately $120,000 annually, totaling more than $1.4 million during the relevant time period, which Silver received based on his official position rather than any work he was expected to perform for clients of the firm, plus (ii) approximately $3.9 million in attorney referral fees, over $3 million of which Silver obtained through a corrupt scheme described in greater detail below, whereby Silver obtained referrals of asbestos cases from a doctor ('Doctor-1') by using his official position to secretly direct $500,000 in State funds to Doctor-1's research and provide additional benefits to Doctor-1 and his family."

Neither Taub nor the law firm faces federal charges.

A story describing the arrangement appeared in The New York Times Jan. 23.

Columbia's website describes Taub as the Vivian and Seymour Milstein Family Professor of Clinical Medicine in the Columbia College of Physicians and Surgeons and as an attending oncologist at Columbia University Medical Center.

TONY HUNTER, **CHARLES SAWYERS**, and **JOSEPH SCHLESSINGER** received the **Frontiers of Knowledge Award in Biomedicine** from the BBVA Foundation for their work in on personalized treatments of cancer.

Hunter helped discover tyrosine kinases, Schlessinger helped identify the principle through which they function, and Sawyers helped bring this knowledge to the clinic through the development of novel cancer therapies. Their contributions served initially to treat a variety of leukemia, but have since given rise to effective therapies for lung and breast cancer, melanoma and lymphomas, among others.

Hunter is director of the Salk Institute Cancer Center; Sawyers is the Human Oncology and Pathogenesis Program Chair at the Memorial Sloan Kettering Cancer Center; and Schlessinger serves as chairman of the Department of Pharmacology at Yale University School of Medicine.

The new treatments, all of them approved in the last ten years, differ from traditional chemotherapy in that they specifically target the mechanisms causing each type of cancer, making them less toxic for the patient.

Imatinib, approved in 2001 and the first of this new class of pharmaceuticals, transformed chronic myeloid leukemia from a fatal cancer into one that is nearly always treatable. The award jury remarked that the three laureates have participated independently in a chain of advances running from "the basic discoveries of tyrosine kinase proteins to clinical applications that save lives."

CANCER TREATMENT CENTERS OF AMERICA and the **National Football League Alumni Association** announced a new partnership to raise awareness among NFL alumni and fans about screening, diagnosis and treatment for prostate cancer. The partnership also calls for CTCA to treat NFL alumni who are fighting the disease.

CTCA will become a sponsor of the NFLA's Super Bowl of Golf, an annual member event that is part of the NFLA's charitable fundraising activities. The partnership launched Jan. 29 with an event at the CTCA hospital in Phoenix, home of this week's big game.

MD ANDERSON CANCER CENTER and **AstraZeneca** announced a multiyear strategic research collaboration to conduct multiple, parallel clinical and clinically related studies in ovarian and other gynecologic cancers, including epidemiological and outcomes studies.

MD Anderson scientists will have access to therapeutic agents in the AstraZeneca pipeline and future studies will be determined by the collaboration at a later date. The collaboration will draw on MD Anderson's Moon Shots Program and the center's Sheikh Khalifa Bin Zayed Al Nahyan Institute for Personalized Cancer Therapy.

THE UNIVERSITY OF CALIFORNIA San Diego School of Medicine and **University of California, San Francisco**, with support from a team of collaborators, launched the **Cancer Cell Map Initiative** to determine how all of the components of a cancer cell interact.

The initiative will be co-directed by Nevan Krogan, director of the UC San Francisco division of QB3, a research institute, and Trey Ideker, chief of medical genetics in the UC San Diego Department of Medicine and founder of the UC San Diego Center for Computational Biology & Bioinformatics.

UCSD's Moores Cancer Center and UCSF's Helen Diller Family Comprehensive Cancer Center will provide access to tissue samples donated by patients being treated for cancer.

The CCMI will provide key infrastructure for the recently announced alliance between UC San Diego Health Sciences and San Diego-based Human Longevity Inc., which plans to generate thousands of tumor genomes from UC San Diego cancer patients. It will also leverage resources and information from NCI, including large databases of cancer genomes and pathways that are being developed in collaboration with the San Diego Supercomputer Center and UC Santa Cruz.

Funding Opportunity

SITC and Merck Offering Immunotherapy Fellowship

The Society for Immunotherapy of Cancer, with support from Merck, is providing funding for cancer immunotherapy research through the SITC-Merck Cancer Immunotherapy Clinical Fellowship

The award, available to individuals holding MD or joint MD/PhD degrees, provides one year of salary, equipment, supplies and fringe benefit support. The award recipient will be recognized at an upcoming SITC annual meeting.

The award is provided by the ForwardFund with an independent educational grant from Merck. More information is available online at www.sitcancer.org. Questions related to the fellowship should be directed to development@sitcancer.org.

Drugs and Targets

FDA Adds WM to Imbruvica Label

FDA expanded the approved use of Imbruvica (ibrutinib) for previously treated patients with Waldenström's macroglobulinemia. The drug received a breakthrough therapy designation for this use.

The FDA initially granted Imbruvica accelerated approval in November 2013 for use in patients with mantle cell lymphoma who received one prior therapy. In February 2014, the FDA granted accelerated approval to Imbruvica for use in patients with previously treated chronic lymphocytic leukemia, and then in July 2014, expanded its use to include treatment of CLL patients who carry a deletion in chromosome 17.

The FDA based its approval of Imbruvica for WM on a clinical study of 63 previously treated participants. All study participants received a daily 420 milligram orally administered dose of the medication until disease progression or side effects became intolerable. Results showed 62 percent of participants had their cancer shrink after treatment (overall response rate). At the time of the study, the duration of response ranged from 2.8 months to approximately 18.8 months.

FDA also granted Imbruvica priority review and orphan product designation for WM. The product's new use is being approved more than two months ahead of its prescription drug user fee goal date of April 17. Imbruvica is co-marketed by Pharmacyclics and Janssen Biotech.

FDA granted orphan drug designation to tarextumab (anti-Notch 2/3, OMP-59R5) for the treatment of both pancreatic cancer and small cell lung cancer.

OncoMed Pharmaceuticals Inc., the drug's sponsor, is currently enrolling patients in a randomized phase II clinical trial of tarextumab with gemcitabine plus Abraxane (paclitaxel protein-bound particles for injectable suspension) (albumin bound) in patients with first-line advanced pancreatic cancer.

In January 2015, OncoMed announced positive final phase Ib clinical and biomarker data from its study of tarextumab in combination with standard of care in pancreatic cancer. Tarextumab was well tolerated with manageable side effects and the three drug combination achieved an overall clinical benefit rate (defined as partial responses and stable disease) of 73 percent. Biomarker analyses showed that among patients

whose tumor samples had elevated levels of Notch3 gene expression suggestions of higher response rates and longer survival were noted. For patients with high Notch3 expression, median progression-free and overall survival were 6.6 months and 14.6 months, respectively.

Tarextumab is a fully human monoclonal antibody that targets the Notch2 and Notch3 receptors. Preclinical studies have suggested that tarextumab exhibits two mechanisms of action: (1) by downregulating Notch pathway signaling, tarextumab has anti-cancer stem cell activity , and (2) tarextumab affects pericytes, impacting the stromal and tumor microenvironment.

Health Canada granted a Class 3 Device License approval for **the xTAG CYP2D6 Kit v3** genotyping assay, developed by Luminex Corporation.

Cytochrome P450 2D6 (CYP2D6) is a clinically important gene that encodes a drug-metabolizing enzyme. CYP2D6 metabolizes greater than 25 percent of the drugs in use today including some cardiovascular and anti-cancer drugs, anti-psychotics, anti-depressants, pain-medications, beta blockers, and antiarrhythmics.

xTAG CYP2D6 Kit v3 is an in vitro diagnostic assay that analyzes a patient's CYP2D6 genotype from DNA extracted from a blood sample and is used to aid physicians in determining therapeutic strategy for drugs metabolized by the cytochrome P450 2D6 gene product. The assay is run on the Luminex 100/200 instrument.

Array BioPharma Inc. reached an agreement with **Novartis Pharma AG** to acquire worldwide rights to encorafenib (LGX818), a BRAF inhibitor currently in phase III development. This agreement is conditional on the closing of transactions announced by Novartis and GlaxoSmithKline PLC on April 22, 2014, which are expected to close in the first half of 2015, and the agreement remains subject to the receipt of regulatory approvals.

Array previously announced a definitive agreement with Novartis to regain global rights to the MEK inhibitor binimetinib, the material terms of which remain in place following this agreement. In order to address competition concerns raised by the European Commission, Array has agreed to obtain an experienced partner for global development and European commercialization of both binimetinib and encorafenib.

Upon satisfaction of all conditions and closing of the deal, Array will acquire global rights to encorafenib. Other than a de minimis payment due to Novartis from Array, there are no milestone payments or royalties payable under this agreement by either party.

Novartis has agreed to provide transitional regulatory, clinical development and manufacturing services as specified below and will assign or license to Array all patent and other intellectual property rights Novartis owns to the extent relating to encorafenib. If Array is unable to find a suitable partner in the prescribed time period, a trustee would have the right to sell such European rights.

Novartis will conduct and fund the COLUMBUS trial through the earlier of June 30, 2016 or completion of last patient first visit. At that time, Array will assume responsibility for the trial, while Novartis will reimburse Array for out-of-pocket costs along with 50 percent of Array's full time equivalent costs in connection with completing the COLUMBUS trial. Novartis is responsible for conducting all other encorafenib trials until their completion or transfer to Array for a defined transition period.

Amgen and its subsidiary **Onyx Pharmaceuticals Inc**., announced the submission of a supplemental New Drug Application to FDA and a Marketing Authorization Application to the European Medicines Agency for **Kyprolis (carfilzomib)** for Injection in relapsed multiple myeloma.

In the U.S., the sNDA is designed to support the conversion of accelerated approval to full approval and expand the current approved indication. In the European Union, Kyprolis received orphan drug designation and the MAA has been granted accelerated assessment.

The sNDA and MAA are based on data from the phase III ASPIRE trial and other relevant data.

Kyprolis is in a class of drugs called proteasome inhibitors and was granted accelerated approval by the FDA in 2012. Kyprolis is also approved for use in Argentina, Israel and Mexico.