THE CANCER LETTER

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THE SEVEN-PER-CENT SOLUTION

A NOVEL PLAN TO DOUBLE THE NCI BUDGET BY 2026

AN ASTOUNDING NEW ADVENTURE IN FUNDING BIOMEDICAL RESEARCH

A New Doubling: Advocates, NCI Seek 7% Boost for Medical Research Funding

By Matthew Bin Han Ong

NIH, NCI and FDA should receive budget increases of at least 7 percent a year, the 2015 Cancer Progress Report by the American Association for Cancer Research recommends.

The NCI Bypass Budget for 2017, published almost simultaneously with the AACR report, requests a series of annual 7-percent increases for NCI, which over a decade would double the institute's budget (The Cancer Letter, Sept. 18).

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Bypass Budget Calls for 7% More in 2017 —and Doubling by 2026

By Paul Goldberg

The NCI Bypass Budget for 2017 asks for a 7-percent increase over fiscal 2016, followed by a series of annual 7-percent increases that would continue through 2026, when the institute's budget would double.

The Bypass Budget is submitted by the NCI director to the U.S. President under a unique authority given to NCI under the National Cancer

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Lowy: Increase for Cancer Center Grants Is Contingent on FY2016 Appropriations

NCI is planning to increase funding for the Cancer Center Core Grants, Acting Director Douglas Lowy said to the National Cancer Advisory Board at a meeting Sept. 16.

"We have had a number of internal discussions since the joint board meeting in June and we are going to be having a meeting of working group of

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Advocates, Legislators Call For Increases to NIH Budget

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The institute and the advocates are making nearly identical requests at a time when the outlook for NCI funding is showing signs of improvement.

• President Barack Obama has proposed a $1 billion increase, the House has proposed a $1.1 billion increase, and the Senate has proposed a $2.2 billion increase.

• If a budget deal raises the caps, NIH would stand receive to receive the largest annual appropriations increase in many years, Capitol Hill insiders say.

• In the 21st Century Cures bill, the House approved an $8.75 billion boost for NIH in mandatory funding over five years through the creation of a new "Innovation Fund." Also, the bill authorized increased funding levels (through the annual appropriations process) for the NIH by $1.5 billion per-year for the next three fiscal years.

NIH has lost nearly 25 percent of its funding since 2003 due to flat budgets and biomedical inflation. As a result, fewer competitive research grants have been awarded, which advocates argue is slowing progress in biomedical research and discouraging young scientists from pursuing a career in research.

In addition to over a decade of flat funding, the Budget Control Act, enacted in March 2013, slashed funding for federal agencies, including NIH, NCI and FDA, by 5.1 percent.

AACR's fifth annual report was released Sept. 16 in conjunction with this year's Rally for Medical Research Hill Day—a two-day event where over 300 organizations across the country converge on Capitol Hill to advocate for sustained increases in funding for NIH. The association is the lead sponsor and founding organizer of the rally, now in its third year.

The US is losing scientists to other countries because of better opportunities abroad, said NIH Director Francis Collins at the rally Sept. 16.

"I was in Korea and China last week, and I met with some amazing scientists, some of which used to be here. They're not here anymore," Collins said at the Reception to Celebrate Medical Research at the Russell Senate Office Building. "There are better opportunities that lie in Asia, because as we have lost ground, other countries have been gaining their momentum.

"If we're serious about doing things to stimulate our economy, the dollars that go into medical research are well documented as one of the best government investments we can make, because of all the spinoffs, all the small businesses, and jobs that get created. If we're serious about American competitiveness, we should worry about this.

"Currently, as young scientists look at our situation, this is a particularly vulnerable time," Collins said. "And we need to be able to give them the reassurance that we are in fact, serious about providing the kind of support, so that when they come to NIH with their best and brightest ideas, their chances won't continue to be 1 in 6 of getting funded, which is what it currently is. We need to be better than that.

"Research can't wait, there are many epidemics that can't wait, cures can't wait, hope can't wait, we can't wait, none of us can wait, and America cannot wait."

Members of Congress: Increase Research Funding

Other speakers at the Sept. 16 reception included Sens. Jerry Moran (R-Kan.), Patty Murray (D-Wash.), Amy Klobuchar (D-Minn.), and Dick Durbin (D-Ill.).

"One of the goals I share with many of my colleagues, including Sen. Murray, is the idea that budget caps are damaging to the research that goes on at NIH, and they change dramatically the opportunity for the United States of America to be the leader in medical research and to develop an economy based on science, and medical research, and we will work to prioritize the spending that occurs at NIH," Moran said at the event.

The life sciences sector in Washington—the fifth-largest sector in the state—employs 34,000 people, and is continuing to grow, Murray said.

"Maintaining our country's central goal of life sciences as a very top priority and the federal investments in medical research are so critical to that effort," Murray said. "I believe we need an agreement that builds on the bipartisan foundation. That was set at our budget deal last Congress, that protect priorities like research and education and our national security."

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Congress should be increasing investment to the NIH, not shrinking it, Klobuchar said.

"One of the issues here is the budget and making sure we continue to invest in NIH, I made that point when I gave my salary to the NIH during the government shutdown, but that's one thing, the other is expanding and growing it," Klobuchar said.

Devoting funds to biomedical research is an indispensable investment in America's future, said Durbin.

"Here's our challenge: there are a bunch of members of Congress who say they're all for increasing federal investment for medical research, but we have to take the money from other places," Durbin said. "Take it out of school lunches, take it out of federal subsidies to help families pay for health insurance, take it out of student loan guarantees.

"Well, I say there's a better solution: lift the budget caps so America remains the world's leader in biomedical research."

Rally participants held a series of meetings with the House and Senate on Sept. 17 to advocate for predictable increases for NIH.

"The American Association for Cancer Research is thrilled that the Rally for Medical Research Hill Day has become such an important event for hundreds of organizations from all across the United States to come together and speak with one voice to Congress about the critical importance of medical research, and encourage Members of Congress support robust, sustainable, and predictable budget increases for the NIH," said Jon Retzlaff, managing director of the AACR Office on Science Policy and Government Affairs. "The time to invest is now. Congress must develop a budget framework that supports stronger investments in the NIH for the long-term."

Despite competing priorities on Capitol Hill, the momentum behind research is gaining strength, said Research!America President and CEO Mary Woolley.

"At the Rally for Medical Research reception, the energy in the room was palpable, fueled by a sense of determination by Senators Durbin, Murray, Klobuchar and Moran to increase and sustain our national commitment to research," Woolley said to The Cancer Letter. "Dr. Francis Collins fired up the advocates with his rousing and frank remarks: patients can't wait, families can't wait and research can't wait.

"This is our moment; our year, and advocates are up to the challenge of assuring elected officials follow through."

Alberto Busch contributed to this story.

Lowy Asks for Doubling for NCI by Fiscal 2026

(Continued from page 1)

Act of 1971. Over the years, the budgets have had different functions, which reflected the priorities—and styles—of the institute directors who submitted them.

Some viewed the Bypass Budget as a weighty scholarly and programmatic document, others as a glossy annual report. One former director saw it as a propaganda vehicle for delivering bombastic promises to end "suffering and death due to cancer by 2015," and on some years occasion the Bypass Budget was skipped altogether.

The core of the 2017 Bypass Budget is brief: a two-page foreword from NCI Acting Director Douglas Lowy and a one-page table showing how NCI would spend additional $355 million that would boost its budget from the 2016 estimated level of $5.098 billion to $5.453 billion.

If the Lowy approach to the Bypass Budget sticks, he and future NCI directors would be able to avoid the headache of an annual exercise in creative writing and instead concentrate on their day jobs.

Lowy's foreword and the table—arguably the principal components that advocacy groups and policymakers look at—are the only sections of the Bypass Budget available in the PDF format. This is the section that went to the White House.

Additional materials are available online.

"Communication is an important step in the scientific process, and NCI takes its responsibility to report about programs and scientific findings very seriously," said Peter Garrett, director of the NCI Office of Communications and Public Liaison. "With the Bypass Budget authority, we have a vehicle for sharing our professional judgment directly with the Administration and Congress by highlighting the scientific opportunities and priorities for cancer research.

"The Bypass budget also gives NCI a way to share this information with the broader cancer community and generate a dialogue with stakeholders. This year, we hope researchers, health providers, and patients will add their perspective about some of the most promising areas for advancing cancer research."

The Bypass Budget request matches the recommendations in the Cancer Progress Report prepared by the American Association for Cancer Research and published earlier this week. (The Cancer Letter, Sept. 18)

In the 21st Century Cures bill, the House approved

a $8.75 billion boost for NIH in mandatory funding over five years through the creation of a new "Innovation Fund." On top of that, the bill authorized increased funding levels (through the annual appropriations process) for the NIH by $1.5 billion per-year for the next three fiscal years.

The text of Lowy's Bypass Budget message follows:

When I speak with leading cancer researchers in the United States and around the world, I hear unprecedented optimism that we are on the verge of pivotal advances in oncology. This sentiment is based on progress in many important areas, including immune-based therapies, genomics, advanced imaging technologies, new laboratory models of human cancer, precision medicine, and more.

Key aspects of our understanding of and approach to cancer have been transformed based on years of investment in biomedical research. We are increasingly able to treat cancer with greater precision by identifying the molecular abnormalities that drive each person's cancer and targeting therapies to each patient, ultimately improving outcomes and providing hope.

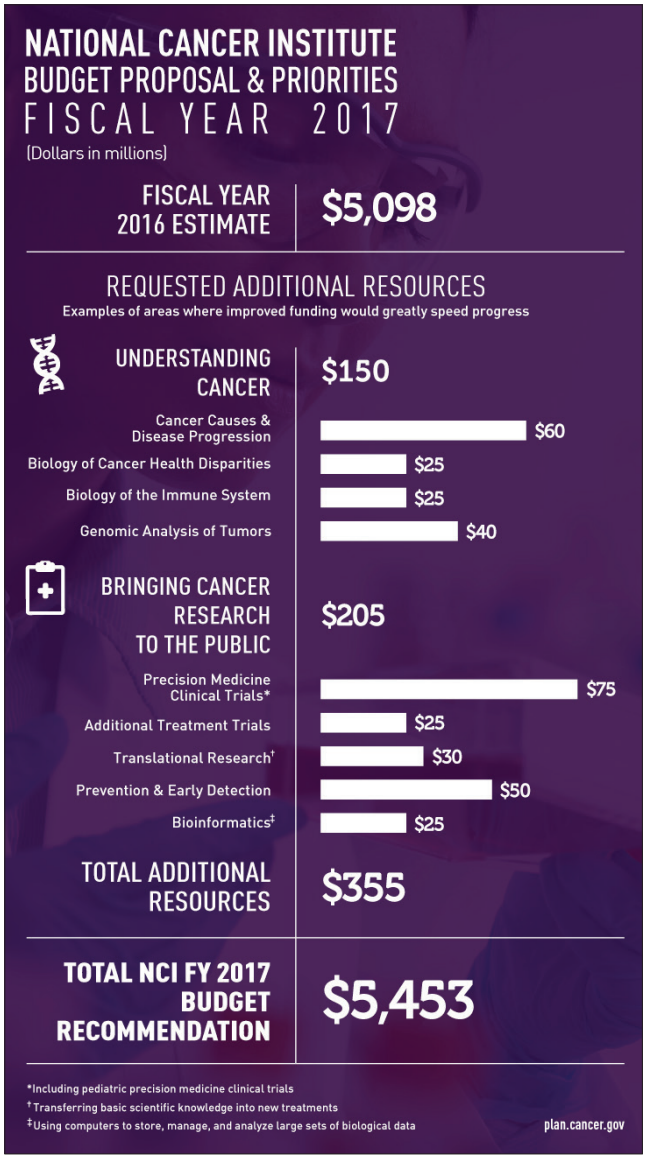
This promise of precision medicine has already been realized for treating some cancers, and we foresee greater progress in preventing, screening, and treating other cancers and even other diseases. Cancer research, therefore, offers a model for other fields of biomedical research that seek to leverage genetic and other molecular information to administer precise and effective interventions to treat disease.

At NCI, we are advancing precision oncology, while managing our resources to take full advantage of the most promising scientific opportunities. It is essential that NCI support the full continuum of scientific research—from basic biological research, to population-based studies, to cutting-edge clinical trials—as virtually all advances in cancer depend on many fields of science.

Although dramatic progress is being made, important scientific opportunities lie before us. With steady and sustained budget increases and a cadre of talented researchers, a new era of cancer medicine is well within reach.

Despite careful management of the NCI budget, many meritorious research proposals—including some bold concepts—must go unfunded each year due to the fiscal constraints we have been operating under for more than a decade. There is little doubt that budget constraints have resulted in missed scientific opportunities.

With the exception of the one-time increase allocated in the American Recovery and Reinvestment Act, federal investment in cancer research has been



stagnant since 2003. During this same period, the costs of conducting research have escalated as inflation has substantially eroded NCI's purchasing power. As a result, competition for NCI grants has been fierce, and some young researchers, frustrated by a lack of funding, have abandoned careers in medical research.

The current budget situation has hindered NCI's ability to optimally fulfill its mission and promise to the American public: to foster rapid progress and reduce the burden of cancer.

Working closely with its advisory boards, NCI senior leadership has made difficult funding choices, reducing funding for some worthwhile programs and initiatives and curtailing funding altogether in some cases.

In the budget table that follows, NCI recommends a funding increase of 7 percent over the fiscal year 2016

level to pursue promising research opportunities that improve our understanding of cancer and reduce the burden of the disease. These research opportunities are among those for which additional funding would greatly speed the progress against cancer.

But a 7 percent increase can only be viewed as an initial down payment. Steady funding increases, sustained over time, are necessary to restore NCI's purchasing power and accelerate scientific discovery in ways that significantly reduce the burden for people with all types of cancer. An annual increase of 7 percent for the next 10 years is necessary to achieve these goals. These steady increases will result in a fiscal year 2026 budget for NCI that is twice what it is today.

As NCI's leader, I am continually inspired by the incredible dedication and passion of the institute's staff and researchers, as well as the dedication and passion of cancer researchers across the country and around the world. We understand that patients and their loved ones expect and deserve continued progress and that we have an obligation

Douglas R. Lowy, M.D.

Acting Director, National Cancer Institute

Raise for Centers Hinges on 2016 Appropriations

(Continued from page 1)

cancer center directors—that's chaired by Stan Gerson [director of Case Comprehensive Cancer Center] and Chi Dang [director of the University of Pennsylvania Abramson Cancer Center] in October, to go over some potential approaches for increasing the award size," said Lowy during his second director's report since he became acting director. "The goal is to try to develop a plan that can be presented at the joint NCAB and BSA meeting at the beginning of December.

"Whatever we do, I'm not going to talk about the FY16 budget, but I just want to point out that it has not been passed, and until it is passed and until we get an increase in our appropriation, we would need to hold in abeyance the commitment for full funding for the increases in order to be fiscally responsible."

The following is a transcript of NCI Acting Director Douglas Lowy's remarks to the National Cancer Advisory Board Sept. 16:

It is a real opportunity for me to try to tell you about some of the things that have happened in the last ten weeks since we had the joint board meeting. I just am going to hit a few highlights, because really the key goal today is to try to go through a number of grant

USPSTF: Aspirin for Cancer Prevention

- Draft report recommends low dose aspirin for ages 50 to 59 to prevent colorectal cancer
- Some unanswered questions:
  - Benefits in those >59
  - Mechanism of action
  - Biomarkers predictive of benefit

applications and try to make decisions about those.

First, I want to mention that FY17 NCI Bypass Budget is going public tomorrow. Those of you who are members of the NCAB have been sent a website, accessible to you today.

I would like to go on and to talk about science with a clinical relevance. With the first slide—I have a total of six slides—this week, the United States Preventive Services Task Force made a draft report that recommended low-dose aspirin for men and women between the ages of 55 and (inaudible) at average risk of colorectal cancer. This is the first time that they have made such a recommendation.

And I want to remind the NCAB that we have had a number of presentations about the research related to aspirin and its potential to reduce the risk of colorectal cancer as well as a number of other cancers.

Barry Kramer [director of the NCI Division of Cancer Prevention] made a presentation a couple of years ago, and Andy Chan [of Massachusetts General Hospital] from Harvard made a presentation even more recently. There are at least three outstanding questions, and I want to emphasize that their report is a draft report—it's open for comment—and what their final recommendation will be remains to be determined.

But from a research perspective, one question is, "What are the benefits in those who are over 59." The second is, "What is the mechanism of action by with aspirin induces this activity?" and the third is trying to identify biomarkers that are predictive of benefit as an approach to try and further increase the benefit to harm ratio and we are supportive of research whose goal is to try to address all three of those areas and I just wanted to highlight, that this is a potentially important change in standard of care, but it is still very much in progress.

The second slide is to talk about the status of some new award types. The Outstanding Investigator Award, we have made the initial awards actually of forty for FY15, and there are going to be subsequently another 24 awards made for FY16 from the initial round.

Status of some new award types

- Outstanding investigator award
  - Initial awards have been made: 64.
  - Reissuance has been published: minor changes (e.g., page length for research strategy reduced from 12 pages to 6 pages)
- Some other types of award under consideration: Research Specialist; Graduate Student to Post-doc

There has been a reissuance of this award, and there are minor changes, perhaps the most salient is the page length for the research strategy has been reduced from 12 pages to 6 pages, but you can go and look at the FOA for details.

In addition, we have been discussing both within the NCI and well as with the NIH other types of awards, and two that I would like to highlight that are not yet quite ready for primetime, but that we hope to be ready in the not too distant future.

Our one for research specialist and the other for the graduate student to postdoc transition, which we hope will help in the very important area of training—a number of new initiatives that we are hoping are going to help our extramural colleagues in their development sustainability and their ability to conduct really cutting-edge research.

The third slide is that we are making progress towards the goal of increasing funding for the NCI Cancer Center Core Grants. We have had a number of internal discussions since the joint board meeting in June and we are going to be having a meeting of working group of cancer center directors—that's chaired by Stan Gerson [director of Case Comprehensive Cancer Center] and Chi Dang [director of the University of Pennsylvania Abramson Cancer Center] in October, to go over some potential approaches for increasing the award size. The goal is to try to develop a plan that can be presented at the joint NCAB and BSA meeting at the beginning of December.

Whatever we do, I'm not going to talk about the FY16 budget, but I just want to point out that it has not been passed, and until it is passed and until we get an increase in our appropriation, we would need to hold in abeyance the commitment for full funding for the increases in order to be fiscally responsible.

As I mentioned at the joint board meeting back in June, one of the areas that we're trying to focus on are cancers with health disparities as very important

Towards Increased funding for NCI Cancer Center P30 Core Grants

- Working group meeting of cancer center directors: October 9; Chairs Stan Gerson and Chi Dang
- Goal: To develop a plan that can be presented at joint NCAB/BSA meeting in December
- Full funding would be contingent on an increased NCI appropriation for FY16

examples of high risk populations, and what to try to do about it. And we're going to be conducting a workshop in the beginning of November, it's going to be in Atlanta, because it's just prior to the AACR conference on cancer health disparities, and we're going to be emphasizing trying to look at biology, lifestyle and access in utilization.

The purpose of this workshop is to try to identify some high-priority areas of research for the NCI to consider supporting. It will bring together what research are we currently supporting and the goal is to try to make our research in this area to be more cohesive, comprehensive and to have an even greater impact than we're currently having. The co-chairs for the conference are Edith Mitchell from Thomas Jefferson University, Lisa Richardson [director of the CDC Division of Cancer Prevention and Control] from the Center for Disease Control and Sandy Markowitz from Case Western Reserve.

In conjunction with this, I should also point out that we have established a new NCI center, which we are calling the Center for Research Strategy, and Michelle Bennett, who used to be a deputy director in the Intramural Center for Cancer Research, but who went to be a deputy director in the Heart, Blood and Lung Institute, has come back to the NCI and she is going to be heading up this center and helping to coordinate the workshop that I'm referring to.

The focus of the center is to focus on trans-NIH activities that span a variety of scientific disciplines, and so we hope that this will be one way of trying to make our research more cohesive than it is already.

Another area in health disparities is something that really has been spearheaded jointly by Sanya Springfield, the director of the NCI Center to Reduce Health Disparities, and Kevin Cullen at the University of Maryland, who heads up the cancer center. And this is the development of a pilot program for middle school students in Baltimore to select about 30 students from

Focus on specific cancers with health disparities (high-risk populations)

- Workshop: November 11-13, in Atlanta, just prior to AACR conference on cancer health disparities: biology, life style, access/utilization
- Co-chairs: Edith Mitchell (Thomas Jefferson University), Lisa Richardson (CDC), Sandy Markowitz (Case-Western Reserve)
- New NCI Center for Research Strategy; Michelle Bennett, director; focus on trans-NCI activities that span scientific disciplines (e.g., health disparities)

Pilot program for Middle School Students in Baltimore

- Administered through University of Maryland Cancer Center
- Developed by Sanya Springfield, Director, NCI Center to Reduce Cancer Health Disparities
- Select ~30 students from 3 schools to learn about biology, cancer, and research: activities at school and at Cancer Center

three schools to learn about the biology, cancer and research and there will be activities at the school as well as at the University of Maryland Cancer Center and I had the pleasure a few weeks ago of going with Sanya up to the University of Maryland and meeting with Jay Perman, the president of the university, and with Kevin and many of his colleagues and to hear something about the program.

Kevin, would you like to tell us briefly about some aspects of it?

KEVIN CULLEN: Thanks. We're very excited about this. I want to thank Sanya and her staff for all their support. This is a program quite literally in the neighborhood of Freddie Gray, and it's really an effort to help the opportunities for kids in the community around our cancer center. We've devised a very intensive mentoring and tutoring program for kids in middle school two afternoons a week and one day on the weekend with the goal of making kids more competitive for advanced training well before they get to college and we were very appreciative of the partnership with Sanya's team in an effort to give back to the community.

I have to say that all of the faculty at the cancer center have been incredibly enthusiastic about participating.

LOWY: I just want to point out that the center that Sanya runs has been promoting the notion of long-term training for these students. So we've gone down as far as the high school level up to now, but this is our first foray into middle school, and the enthusiasm that was expressed when we visited the University of Maryland was quite impressive.

The last areas that I want to touch upon—and as Tyler said, I will turn the microphone over to Jim Doroshow [director of the NCI Division of Cancer Treatment and Diagnosis]—is the Precision Medicine Initiative in oncology. We had an excellent, vigorous discussion about this at the joint board meeting in June, and we have continued to try to refine and develop it, and we also certainly listened to that discussion and some of the questions and comments that were made there and in other venues.

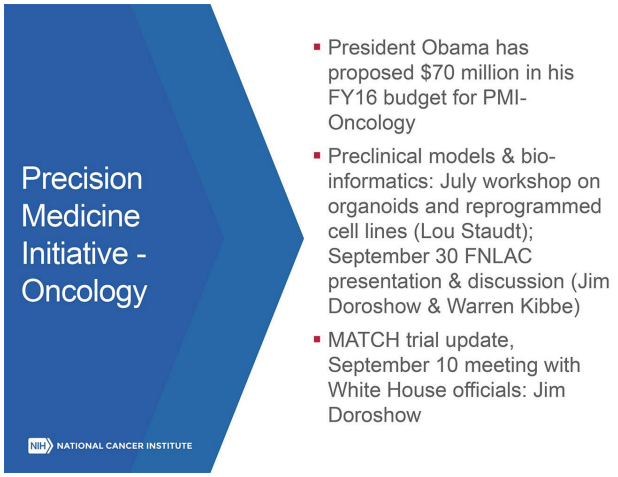
We have had a workshop on organoids and reprogrammed cell lines that Lou Staudt [director of the Center for Cancer Genomics] organized—that was in July and it was an international workshop with investigators, especially from the United Kingdom and from the Netherlands, participating. At the end of this month, the Frederick Advisory Committee is going to be hearing a presentation from Jim Doroshow on the PMI initiative in general and also on preclinical models, and as well from Warren Kibbe [director of the NCI Center for Biomedical Informatics] on the bioinformatics aspect of it.

The MATCH trial, which was one of the aspects that was highlighted at the June joint board meeting, has now opened, and Jim also went to a meeting last week that was organized for White House officials. Jim is going to give us an update on the MATCH trial and that meeting at the White House.

JAMES DOROSHOW: Many thanks, Doug. First, I want to thank all of the individuals across the country who have made the launch of the MATCH trial, not only a major undertaking, but a major success.

As many of you know, the trial was actually open to accrual just a few weeks mid-late August. The first two weeks, 60 patients were accrued and accrual continues at the initial 400 plus sites that opened the trial and we expect to actually get close to the 2,000 plus sites in a relatively short period of time.

The initial trial opened with 10 therapeutic arms under the MATCH umbrella. By either the end of this month, or very early in October, another nine clinical trials will be approved, and then several more rapidly thereafter. We think that we will get to at least to the 22 trials stage under the MATCH umbrella relatively soon,



and certainly by the end of October.

You might be interested in the following, that is the initial accrual, most of it has actually been at our community sites that have been very interested in participating and have shown their ability to obtain fresh tumor biopsies in the community and get those materials to our quality control site at MD Anderson, and then to have the analyses performed.

I would be absolutely remiss if I didn't say a word about what has been a remarkable collaboration between NCI staff and the ECOG-ACRIN staff that have made the processing of materials in as short as nine to 10 days from the time of biopsy possible with a great deal of work in the middle, over the past year and a half to make that happen.

We're very happy that this has launched so well, we're very hopeful that the accrual continues, and we will continue to negotiate; and we are continuing to negotiate with a variety of additional pharmaceutical concerns to bring new arms under the MATCH umbrella.

Let me say a very brief word or two about last Friday—I was fortunate enough to brief a group of White House staff about not just the MATCH trial, but also the oncologic aspects of the Precision Medicine Initiative and they were very, very supportive, very interested—not only the clinical trials aspects that we hope to continue and expand, in fact, as new observations are made in the context of NCI MATCH, but also the basic attempt to try to develop more models that are relevant to both drug resistance and to a variety of tumors that are not well represented in current collections of PDX and other models for cell lines and xenografts.

I don't think Dr. Kibbe knows this, but the most questions that I got were on the IT aspects of the Precision Medicine Initiative. I did the best I could under the circumstances—I'm just delighted that I know what a petabyte is—but they're going to contact Warren more for further information.

TYLER JACKS [director of the Koch Institute for Integrative Cancer Research at MIT]: Thank you, Doug and thank you, Jim. The floor is open for questions for both Doug and for Jim.

Maybe I'll start with one briefly. Doug, I know you won't want to give great detail about your thoughts of increasing budgets for cancer centers, especially before the group next meets.

But if you could give us a sense of order of magnitude changes here: What kind of increases, broadly speaking, are you expecting might occur?

LOWY: I think that we are looking to try to increase the budgets by 15 to 20 percent.

JACKS: Thank you. Other questions?

MARCIA CRUZ-CORREA [director of the Gastrointestinal Oncology Program at the University of Puerto Rico Cancer Center]: Hi everyone. First of all, thank you for sharing this information with us. I was really excited to hear about the program that is being led in collaboration with Dr. Springfield and the Center for Cancer Health Disparities. Thank you for working on that. I have to tell you that I think we may have also participated in similar programs, not for high school students, but for the grad students, so again, congratulations on that effort. I'm a part of some of that so thank you for working on that.

It was mentioned that there's a research specialist award—do you have a date?

LOWY: We don't have a date yet, which is why I was trying to be somewhat vague. We are hopeful that there will be signoff and we'll be able to have this pilot program up and running in the near future.

CRUZ-CORREA: That's very much needed. Thank you.

OLUFUNMILAYO OLOPADE [director of the University of Chicago Center for Clinical Cancer Genetics]: Doug, thank you for your emphasis on developing a strategy to reduce disparities, and I particularly like it because you're sort of putting this as priority at the same time that we're putting Precision Medicine as a priority.

In view of the report on the NCI MATCH trial where you have actually good accrual from the community, I'm just curious as to the strategy of getting more resources in the community to be able to participate in the MATCH trial in terms of an expanded network that actually covers more geographically diverse community practices that could potentially

bring in diverse populations to participate in NCI clinical trials.

DOROSHOW: I don't have whole answer to your questions, but I have a little of an answer and that is that a couple months ago, actually spurred on by Dr. Cruz, we had a teleconference with several institutions to have a specific navigator program that's well developed—one of them being UAB, and there are others.

Basically, we decided after that meeting to provide additional support for their navigator programs, specifically to enhance accrual in underserved populations to the MATCH trials. We were able to provide administrative supplements at the end of, well, we have done it this year to try specifically, and I think that's one way where there are already infrastructures that possibly I have a track record, we could add resources specifically to assist in accrual to NCI MATCH.

LOWY: Funmi, let me respond to a related question that you didn't ask about, because it was a comment made at the joint board meeting, which was, with the preclinical models that we should also pay close attention that underrepresented minorities are well represented in those preclinical models, and we have taken that concern to heart.

OLOPADE: Thank you.

LOWY: In closing, I just want to reiterate what I said at the beginning about the bypass budget, that it will publicly available tomorrow. It's going to be different in its format from what it has been before. There will be a bypass budget online, similar to last year's but it will be much more Internet user-friendly and there will be hyperlinks, videos etc.

If you like it, you should please compliment Peter Garrett [director of the Office Communications and Public Liaison] and his colleagues if you like the text. Rick Manrow [associate director of the Office of Cancer Content Management] has provided a tremendous amount of effort in a very short turnaround time, and if you don't like it, complain to me.

Robert Califf Tapped for FDA Commissioner Position

By Paul Goldberg

President Barack Obama nominated Robert Califf to the post of Commissioner of Food and Drugs.

Earlier this year, Califf was named FDA Deputy Commissioner for Medical Products and Tobacco, a de facto No. 2 post at the agency. Califf, 63, is an expert in cardiology, clinical research, and medical economics.

Califf, 63, spent the preceding 33 years at Duke University, most recently as vice chancellor of clinical and translational research.

At FDA, he oversaw the 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.

Califf has said that 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.

"We believe that with Dr. Califf's diverse background, and his exemplary knowledge of clinical and translational medicine, he will continue to improve the FDA's drug approval process while ensuring that patients are receiving the safest and most effective treatments as quickly as possible," Friends of Cancer Research, a Washington group, said in a statement. "Friends looks forward to working with Dr. Califf on vital issues that directly impact patients' lives and to being a resource to help drive FDA's commitment to personalized medicine, and enhance the agencies engagement with stakeholders and patients."

Biotechnology Industry Organization President and CEO Jim Greenwood commended the President for nominating Califf and urged the Senate to consider his confirmation as soon as possible.

"Dr. Califf is a respected cardiologist and clinical trial expert with a firm understanding of the challenges and opportunities of 21st century medicine," Greenwood said. "The FDA deserves a strong, confirmed Commissioner to effectively fulfill its expanding obligations and maintain appropriate standards for the safety and effectiveness of advanced therapies."

Michael Carome, Director, Public Citizen's Health Research Group, urged the Senate to reject Califf.

"His nomination undoubtedly comes as welcome news to the pharmaceutical and medical device manufacturers, but is bad news for patients and public health," Carome said. "During his tenure at Duke University, Califf racked up a long history of extensive financial ties to multiple drug and medical device companies, including Amgen, AstraZeneca, Eli Lilly, Johnson & Johnson, Merck Sharp & Dohme and Sanofi-Aventis, to name a few. Strikingly, no FDA commissioner has had such close financial relationships with industries regulated by the agency prior to being appointed.

"Califf's appointment as FDA commissioner would accelerate a decades-long trend in which agency leadership too often makes decisions that are aligned more with the interests of industry, rather than those of public health and patients."

NCI Funds Five Teams To Work With Animal Models for Children's Cancer

NCI has funded five research teams to participate in its Pediatric Preclinical Testing Consortium.

The consortium is designed to focus on preclinical models in order to help prioritize agents for entry into clinical trials.

"Effective prioritization of potential drug candidates is critical," Malcolm Smith, associate branch chief of Pediatrics in NCI's Cancer Therapy Evaluation Program, said in a statement. "There is a large universe of anticancer agents being developed for adult cancers, but because of the relatively small number of children with specific cancers, only a limited number of these agents can be studied in pediatric clinical trials."

The five research teams were selected to conduct preclinical testing for childhood cancers based on their experience and on the preclinical models that they have previously developed. The principal investigators of each research team are:

• Richard Gorlick, Albert Einstein College of Medicine: Osteosarcoma

• Peter Houghton, Greehey Children's Cancer Research Institute. (Sarcoma and renal cancers.)

• Xiao-Nan Li, Baylor College of Medicine. (Brain cancers.)

• John Maris, Children's Hospital of Philadelphia. (Neuroblastoma.)

• Richard Lock, Children's Cancer Institute of Sydney, Australia. (Leukemia.)

"The primary rationale for this consortium is the fact that there are very few new drugs for pediatric cancer, and many of those drugs that have been introduced have been dependent on the results of clinical trials in adults," CHOP's Maris said in a statement. "Before testing a drug in children, we need a scientific basis for using it, based on deep understanding of the biology involved, and supported by promising results in cell and animal models. These preclinical findings will provide stronger evidence for us to engage proactively with drug companies who could partner in developing these drugs."

The consortium follows on the work of the Pediatric Preclinical Testing Program (PPTP), a decade-long initiative in which NCI worked with more

than 50 pharmaceutical companies to test novel agents in PPTP-provided preclinical models.

One of the most important findings from the PPTP was that many agents that have shown efficacy against adult cancers had limited activity in pediatric preclinical models.

Some investigational drugs did show substantial activity in several models, however, including the MEK inhibitor selumetinib in gliomas with mutations in the BRAF gene and the PARP inhibitor talazoparib (in combination with low-dose temozolomide) for Ewing sarcoma. Both of these agents are now being tested in ongoing pediatric clinical trials.

The PPTP and other research teams have also shown that preclinical testing, when combined with knowledge about the relative drug exposures that can be tolerated by mice and humans, "provides powerful insight into the likely clinical utility of experimental agents," Smith said in a statement.

Research Triangle Institute is the coordinating center for the PPTC.

In Brief

Jones, Parwani Recruited to Key Roles in Ohio State Wexner Pathology Programs

DAN JONES and **ANIL PARWANI** were recruited to serve in leadership roles for specialized pathology services offered across T**he Ohio State University Wexner Medical Center**.

Jones will serve as vice chair and director of molecular pathology in the Department of Pathology and as director of molecular pathology for The Ohio State University Comprehensive Cancer Center—Arthur G. James Cancer Hospital and Richard J. Solove Research Institute.

Parwani, was appointed vice chair and director of anatomic pathology in the Department of Pathology. In addition, Parwani will serve as the director of a new shared core facility focused on digital pathology imaging and pathology informatics.

Jones most recently served as medical director of cancer diagnostics devices at the Quest Diagnostics Nichols Institute, where his group was responsible for the development of more than 100 oncology, genomics and pathology assays. Previously, at MD Anderson Cancer Center, he was a tenured professor overseeing a research laboratory and the clinical molecular diagnostics team that served 13 cancer care centers. In this role, he also designed molecular monitoring protocols for clinical trials.

Jones has authored more than 250 scientific manuscripts and book chapters, emphasizing advanced diagnostics and the molecular basis of leukemia and lymphoma as well as molecular modeling of outcome and response to standard therapies in colon cancer, melanoma and other solid tumors.

Parwani arrives from the University of Pittsburgh, where he served as a professor of pathology and biomedical informatics and director of the division of pathology informatics.

In his new role as vice chair and director of anatomic pathology, Parwani will focus on automation and standardization of anatomical pathology operations including implementation of bar coding and tracking solutions within the laboratory information system.

At OSUCCC-James, Parwani will direct the digital pathology service focused on expanding precision cancer diagnostics and treatment. Parwani has published more than 250 peer-reviewed articles and several books and book chapters focused on the digital pathology, pathology informatics, diagnostic and prognostic markers in genitourinary pathology and molecular classification of kidney cancer.

BROAD INSTITUTE and **MD ANDERSON CANCER CENTER** were designated the **Genome Characterization Centers** in a five-year project supported by the NCI to characterize the genomic changes found in tumors.

GCC's funding comes via a research subcontract with Leidos Biomedical Research Inc., operations and technical support contractor for NCI's Frederick National Laboratory for Cancer Research.

The centers will provide Whole Genome, Whole Exome and RNA sequencing to support three main project areas:

• The Exceptional Responders Initiative aimed at discovering and understanding the molecular events involved in extraordinary individual responses to otherwise unsuccessful targeted experimental cancer therapies.

• The ALCHEMIST Project (Adjuvant Lung Cancer Enrichment Marker Identification and Sequencing Trials) aimed at providing molecular data to support biomarker classification and genomic characterization of lung cancer patients enrolled in clinical trials.

• The Cancer Driver Discovery Project aimed at

providing additional statistical power to discover driver mutations in lung, colon and ovarian cancer.

The project was funded under Contract No. HHSN261200800001E.

ROBIN DAVISSON was named president and CEO-elect of the **Melanoma Research Alliance** effective Oct. 1.

Davisson, the Andrew Dickson White Professor of Molecular Physiology at Cornell University, brings to MRA more than 25 years of internationally recognized scientific research and deep engagement in graduate student and postdoctoral education and mentoring.

She was recently elected a Fellow of the American Association for the Advancement of Science. She recently served as the director of graduate studies of the Molecular and Integrative Physiology field at Cornell for seven years.

Prior to joining Cornell, Davisson was a tenured member of the faculty of the University of Iowa where she taught and researched neuroscience, cardiovascular physiology, and genomics.

"Robin's track record of research and leadership will guide MRA into its next phase as we look to advance the organization and our impact on the field of melanoma research," said Debra Black, MRA co-founder and chair. "Recent landmark advances in melanoma treatment have provided new options for patients, but existing therapies still benefit too few. With Robin at the helm, MRA is poised to accelerate strategic, collaborative, and accountable research efforts needed to advance cures and prevent more melanoma."

Davisson's engagement with MRA will be phased in gradually throughout 2015 and into 2016 as she fulfills her commitments at Cornell University.

MD ANDERSON CANCER CENTER and **Esperance Pharmaceuticals Inc.** entered into a strategic alliance to accelerate the clinical development of its lead anti-cancer candidate, EP-100, for the treatment of ovarian cancer, and to collaborate on preclinical studies of EP-100 as a treatment for breast cancer.

At the 2015 ASCO Annual Meeting, the company reported positive results from a phase II trial of EP-100 in ovarian cancer patients resistant to paclitaxel. EP-100 is a targeted membrane-disrupting peptide designed to seek and destroy cancer cells that overexpress luteinizing hormone releasing hormone receptors on their surfaces. LHRH receptors are over-expressed in a wide range of cancers including ovarian, breast, prostate, pancreatic and endometrial cancer.

MD Anderson will conduct additional studies to help prepare for a phase III trial of EP-100 in ovarian cancer, including more fully elucidating its mechanism of action and identifying potential biomarkers to support the selection of those patients most likely to respond to the drug.

It also will collaborate with Esperance to conduct studies needed to initiate clinical trials of EP-100 in breast cancer and assess the anti-cancer potential of other drug candidates generated by Esperance's Cationic Lytic Peptide platform technology. Further details of the agreement were not disclosed.

Drugs and Targets

AbbVie Submits sNDA for Imbruvica in CLL Patients

AbbVie has submitted a supplemental New Drug Application to FDA based on the randomized, multi-center, open-label phase III RESONATE trial of IMBRUVICA (ibrutinib) versus chlorambucil in treatment-naive chronic lymphocytic leukemia patients aged 65 years or older.

AbbVie announced top-line findings from the trial showing that IMBRUVICA improved progression-free survival and multiple secondary endpoints including overall survival and overall response rate in treatment-naive patients with CLL.

IMBRUVICA is approved for the treatment of patients with CLL who have received at least one prior therapy and CLL patients (including treatment-naive) who have del 17p, a genetic aberration that occurs when part of chromosome 17, the location of the tumor suppressor gene p53, has been lost or deleted.

The RESONATE-2 trial is a Pharmacyclics-sponsored study and its protocol and specific performance goals were established in a special protocol assessment (SPA) with the FDA. An SPA is an agreement with FDA that a phase III clinical trial design, its clinical endpoints and statistical analyses are acceptable to the Agency to support a submission and potential approval.

The trial enrolled 269 treatment-naive patients with CLL or small lymphocytic lymphoma (SLL) aged 65 years or older in the U.S., EU and other regions. Patients were randomized to receive either ibrutinib 420 mg orally, once daily until progression or unacceptable toxicity, or chlorambucil on days 1

and 15 of each 28-day cycle for up to 12 cycles. The starting dose for chlorambucil in Cycle 1 was 0.5 mg/kg and was increased based on tolerability in Cycle 2 by increments of 0.1 mg/kg to a maximum of 0.8 mg/kg.

The primary endpoint of the study was PFS as assessed by an Independent Review Committee according to the International Workshop on Chronic Lymphocytic Leukemia 2008 criteria, with modification for treatment-related lymphocytosis. Key secondary endpoints included ORR, OS and safety.

Can-Fite BioPharma Ltd. of Petach Tikva, Israel, said FDA has granted the company's drug candidate CF102 Fast Track designation as a second line treatment for hepatocellular carcinoma (HCC), the most common form of liver cancer. CF102 had already received the FDA's Orphan Drug designation.

Can-Fite is conducting a phase II study for this indication in the U.S., Europe and Israel. The randomized, double-blind, placebo-controlled study is expected to complete enrollment by the end of the first half of 2016 in 78 patients with Child-Pugh Class B cirrhosis who failed the only FDA approved drug on the market, Nexavar (sorafenib).

Drugs that receive Fast Track designation benefit from more frequent meetings and communications with the FDA to review the drug's development plan to support approval. It also allows the Company to submit parts of the New Drug Application on a rolling basis for review as data becomes available. Since the Fast Track Program started, from March 1998 through June 30, 2015 a total of 318 Fast Track applications have been received by FDA. The FDA has granted 202 of them, and denied 110, with 6 more pending.

CF102 is a small orally bioavailable drug that binds with high affinity and selectivity to the A3 adenosine receptor (A3AR). A3AR is highly expressed in tumor cells whereas low expression is found in normal cells. This differential effect accounts for the excellent safety profile of the drug. In Can-Fite's pre-clinical and clinical studies, CF102 has demonstrated a robust anti-tumor effect via deregulation of the Wnt signaling pathway, resulting in apoptosis of liver cancer cells.

BTG plc of London said that Wellstat Therapeutics' new drug application for uridine triacetate has been accepted for review by FDA.

The sponsor seeks approval of uridine triacetate as treatment for patients at risk of serious toxicity following an overdose of the chemotherapy agent 5-fluorouracil and patients exhibiting symptoms of serious toxicity within 96 hours of 5-FU administration.

FDA has provided an anticipated Prescription Drug User Fee Act action date in March 2016. Uridine triacetate is being developed by Wellstat Therapeutics. If approved by FDA, BTG will market, sell and distribute uridine triacetate for this indication in the US. Wellstat Therapeutics retains certain rights to exercise an option to co-promote uridine triacetate. Terms of the co-promote have not been disclosed.

In 2009, uridine triacetate received orphan drug designation from FDA as an antidote in the treatment of 5-fluorouracil poisoning and from the European Medicines Agency as a treatment for 5-fluorouracil overdose. Under an expanded access protocol, FDA emergency treatment provisions in the US, and similar emergency use provisions in Europe and the rest of the world, uridine triacetate is currently provided to patients at risk of excess 5-FU toxicity due to overdose and patients exhibiting serious toxicities to 5-FU within 96 hours of 5-FU administration. The NDA for uridine triacetate is based in part on efficacy and safety data from U.S. sites in this protocol.

Published literature suggests that each year, approximately 250,000 to 300,000 patients in the US receive multiple treatments with 5-FU, of which 0.5 percent die from 5-FU toxicity. An estimated 10-20 percent of those patients develop serious, sometimes life threatening, 5-FU toxicity or experience an overdose. Non-fatal 5-FU toxicities can result in hospitalization, intensive care utilization and delays in or discontinuation of chemotherapy.

Uridine triacetate is converted in the body to uridine, a direct biochemical antagonist of 5-fluorouracil toxicity.

FDA and the European Medicines Agency accepted regulatory applications for Gilotrif (afatinib), sponsored by Boehringer Ingelheim, for the treatment of advanced squamous cell carcinoma of the lung, after treatment with first-line chemotherapy.

Gilotrif has also been granted Orphan Drug Designation by the FDA.

The submissions are based on positive data from the phase III LUX-Lung 8 study that showed a significant delay in progression of lung cancer and a significant improvement in overall survival for Gilotrif compared to Tarceva (erlotinib).

Data from LUX-Lung 8 showed that treatment with Gilotrif resulted in superior progression-free survival, reducing the risk of cancer progression by

19 percent, and superior overall survival, reducing the risk of death by 19 percent, compared to Tarceva in this patient population.

More patients had improved overall health-related quality-of-life with Gilotrif than with Tarceva (36 vs. 28 percent). Significantly more patients had an improvement in cough with Gilotrif than with Tarceva (43 vs. 35 percent).

Afatinib, an oral, once daily EGFR-directed therapy, is currently approved in more than 60 countries for the first-line treatment of specific types of EGFR mutation-positive NSCLC (under brand names Gilotrif and Giotrif). Approval of afatinib in this indication was based on the primary endpoint of PFS from the LUX-Lung 3 clinical trial where afatinib significantly delayed tumor growth when compared to standard chemotherapy.

In addition, afatinib is the first treatment to show an OS benefit for patients with specific types of EGFR mutation-positive NSCLC compared to chemotherapy. A significant OS benefit was demonstrated independently in the LUX-Lung 3 and 6 trials for patients with the most common EGFR mutation (exon 19 deletions) compared to chemotherapy.

AstraZeneca and Peregrine Pharmaceuticals Inc. entered into a cancer immunotherapy clinical trial collaboration.

The collaboration will evaluate Peregrine's investigational phosphatidylserine-signaling pathway inhibitor, bavituximab, in combination with AstraZeneca's investigational anti-PD-L1 immune checkpoint inhibitor, durvalumab. The planned phase I/Ib trial will evaluate the safety and efficacy of bavituximab in combination with durvalumab in multiple solid tumors. Peregrine and AstraZeneca will collaborate on a non-exclusive basis.

The phase I part of the trial is expected to establish a recommended dose regimen for the combination and the phase Ib part of the trial will assess the safety and efficacy of the investigational combination. Under the terms of the agreement, the initial trial will be conducted by Peregrine.

Bavituximab targets and modulates the activity of phosphatidylserine, an immune-suppressive molecule expressed broadly on the surface of cells in the tumor microenvironment. Durvalumab is a monoclonal antibody directed against programmed cell death ligand 1. Preclinical data have demonstrated that combining the enhanced T-cell mediated anti-tumor activity of bavituximab with checkpoint inhibitors, like PD-L1 antibodies, prolong the ability of tumor-specific T-cells to continue attacking the tumor.

ICON, a provider of drug development solutions, said it's working with IBM to help reduce the time and costs of drug development while also offering patients enhanced quality of care by connecting them to relevant clinical trials. ICON said it will tap Watson's cognitive computing power to help the process of identifying patients who meet the criteria for a clinical trial, and to analyze protocols to assess trial feasibility and identify optimal trial sites.

Initially, ICON is applying Watson Clinical Trial Matching to its breast, lung, colon and rectal cancer trials.

The solution enables ICON to advise sponsors how many patients match their trial criteria, where they are located and how they will recruit them.

IBM's Watson Health Cloud will facilitate access to de-identified patient data, including 50 million patient records contained in the data set from Explorys. At the same time, ICON enhances IBM Watson's capabilities by providing expertise into clinical trial protocols and clinical operations.

More than $1.3 billion is spent on patient recruitment by drug developers each year and yet fewer than 5% of cancer patients participate in a clinical trial. It takes 6-12 months to start up a global phase III drug trial and another 12 months to enroll the required number of patients.

"Recruiting the required number of patients for clinical trials is a constant challenge for our customers and can represent more than 30% of total study costs. ICON's Chief Operating Officer, Steve Cutler, said in a statement. "By applying IBM Watson to our clinical trials, we have the potential to revolutionize clinical trial feasibility, patient recruitment and study start-up timelines which will help our customers take significant time and cost from their development programs."