THE CANCER LETTER

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Guest Editorial

The Moonshot: A View from Europe

By Peter Boyle

"And I believe we need a moonshot in this country to cure cancer."

With these words, Vice-President Joe Biden gave the first public hint of a new specific, major program to be launched and funded by the U.S. government.

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NCI's New Genomic Platform Seeks to Enable Data Sharing for Biden's Moonshot

By Matthew Bin Han Ong

NCI is preparing to open the Genomic Data Commons, a $20 million big data endeavor aimed at making raw genomic data publicly available.

The GDC, NCI's largest bioinformatics effort since the ill-fated caBIG, will go live June 1. The database will be interoperable and publicly available to qualified researchers. Anyone will be able to submit data for consideration.

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Conversation with The Cancer Letter

NCI's Staudt and Kibbe: Data Commons Will Publish Annotated Raw Genomic Data

The Genomic Data Commons, NCI's latest big data project, is poised to become a major player in oncology bioinformatics when it opens June 1.

The GDC aims to become oncology's go-to database for comprehensive, raw genomics information. NCI officials said this sets the GDC apart from other bioinformatics projects, which are vying to play a role in the White House moonshot initiative.

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NCI Platform to Set Moonshot Data Sharing Standards

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While work on the GDC began over two years ago, the initiative is being launched at a time when leading oncology groups are positioning themselves to play a central role in the White House's moonshot initiative.

"The GDC is unique in many ways, and I'll tell you an important one: we are keeping all the raw data, and we keep it in a controlled access way that allows researchers who have the permissions and acumen to look at it," said Louis Staudt, director of the NCI Center for Cancer Genomics.

The Cancer Letter had a conversation with Staudt and Warren Kibbe, NCI acting deputy director and director of the NCI Center for Biomedical Informatics and Information Technology, which appears on page 1.

Planning for a large, more permanent data commons began in late 2013, when it became clear to NCI officials that the amount of cancer genomics data was so immense that it exceeded the limits of CBIIT's data systems.

The GDC is funded as a subcontract awarded by the NCI's principal contractor, Leidos Biomedical Research Inc. Leidos also runs the institute's Frederick National Laboratory for Cancer Research.

In 2014, NCI issued a "best value competitive solicitation" for subcontractors and selected the University of Chicago to develop the GDC.

Robert Grossman, chief research informatics officer and professor of medicine at the University of Chicago, is leading the project. Grossman recruited the Ontario Institute for Cancer Research to build the GDC's user interface.

About 25 reviewers, who made up a source evaluation group, were convened to oversee the acquisition process. NCI officials said the reviewers are experts from government, public, private, commercial, and educational institutions.

"It is Leidos's practice not to release the detailed steps and names of individual reviewers involved in acquisitions, for reasons of confidentiality," Staudt said.

The overarching goal of the GDC is to establish a clinically useful central repository of the molecular taxonomy of cancer, a consolidated data portal that will integrate and store the diverse datasets from CCG's programs.

The database will contain genomic sequences and analyses of tumors, as well as clinical data on enrollment and treatment.

Initially, the GDC will house data from: Cancer Genome Characterization Initiative; The Cancer Genome Atlas; Therapeutically Applicable Research to Generate Effective Treatments, or TARGET; and The Cancer Cell Line Encyclopedia.

Eventually, the GDC will be available as an access point for data from other cancer genomic initiatives. Researchers will be able to use the database to mine information from the GDC and combine it with data from their own research or with data obtained from third parties.

"I think the GDC is a great platform for people to do data sharing and that's really what it's designed to enable," CBIIT's Kibbe said to The Cancer Letter. "What we'd really like to see is all the groups that are out there collecting these kinds of data, that they actually have a place for them to share it."

Staudt said the GDC's ultimate objective is to set standards on a global scale.

"Everybody likes the GDC," Staudt said to The Cancer Letter. "Given the complexity of setting standards on a global scale, there is a real appreciation that what we're developing in the GDC might help drive the conversation in the Global Alliance for Genomics and Health as much as anything else. It is clear that the GDC is going to be part of the solution."

The GDC will be valuable to cancer researchers, said Joyce Niland, chair of the Department of Information Sciences, chief research information officer, and associate director for cancer informatics at City of Hope Comprehensive Cancer Center.

"I think our investigators would use the GDC—it's useful in that it combines all these different efforts," Niland said to The Cancer Letter. "I could see us

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participating in data sharing with the GDC, as long as we have all the right security, safety, confidentiality and permission protocols in place.

"Raw data is highly valuable. That's what makes the GDC so critical. You can't do new experimental analyses without the raw data."

The GDC appears to be a more targeted effort compared to caBIG, said Niland, who is not involved in oversight of the GDC.

"I think lessons were learned from caBIG," Niland said. "One of the things caBIG was trying to achieve—I don't think we ever got there completely, it's very difficult—is to standardize the phenotypic data and the clinical data and to collect that data in an encoded way.

"Genomic data can only be highly valuable and completely useful with the rich phenotypic and clinical data that goes with it—NCI seems to be doing that with the GDC, which is good, and hopefully the extent of these data will be sufficiently rich," Niland said. "You can detect certain patterns and variations with genomic data, but to truly interpret that variation that defines precision medicine and to work on the moonshot, you really need to know what the clinical data and information are."

Several groups are involved in overseeing and reviewing the GDC project: the GDC Steering Committee, the GDC Bioinformatics Advisory Group, GDC Subject Matter Experts, Leidos Biomedical Research Inc. team, and NCI leadership.

The GDC Steering Committee serves as the primary oversight body. Composed of members from academia and cancer research centers, it reviews GDC activities and resources and provides guidance.

The GDC Bioinformatics Advisory Group and Subject Matter Experts provide the GDC with advise on bioinformatics pipelines supporting DNA and RNA sequence alignment to the genome, and the generation of higher-level data such as germline variants and somatic mutations, expression levels of messenger RNAs and microRNAs, and DNA copy number alterations.

The Leidos team and members from NCI leadership support the overall management and execution of the GDC.

The names of the individuals involved in providing oversight for the project appear below.

NCI: We're Doing Something Different

NCI officials say they hope the GDC will help meet the goals of the National Cancer Moonshot Program, a $1 billion initiative led by Vice President Joe Biden.

The moonshot, announced by President Barack Obama Jan. 12, aims to conduct a decade's worth of cancer research over the next five years—primarily by breaking down data siloes and facilitating the creation of a central bioinformatics database for oncology (The Cancer Letter, Jan. 22).

The administration's proposal establishes a game plan for spending the funds: the moonshot initiative will begin with $195 million in cancer research at NIH in fiscal 2016, according to the White House.

Though initial funding is relatively modest by comparison with the overall federal spending on biomedical research, the moonshot is shaping up as a broad-based research and public health initiative.

The administration's budget proposal for the 2017 fiscal year would allocate $755 million in mandatory funds for new cancer-related research activities—$680 million for NIH and $75 million for FDA. The remaining $50 million is expected to fund Centers of Excellence in the Departments of Defense and Veterans Affairs.

"When we've been talking about the GDC and the cloud pilots, and both of those come up with the vice president's office, they're very interested in how we can really use what we've been developing to push the cancer data sharing agenda," Kibbe said to The Cancer Letter. "What the vice president's been saying is we need to make these data available, and discoverable, and we need to learn from all the data that's been generated across the country."

NCI officials say the GDC is distinct from other prominent initiatives that are on Biden's radar, including:

• **The American Society of Clinical Oncology's CancerLinQ.** Launched in 2010, CancerLinQ is expected to use patient care data from millions of physician and patient records from practices and hospitals to provide feedback and clinical decision support to care providers. When the system is completed, doctors will be able to receive personalized insights based on up-to-date findings (The Cancer Letter, Feb. 20, 2015).

• **The American Association for Cancer Research's Project GENIE, for Genomics, Evidence, Neoplasia, Information, Exchange.** The initiative, a multi-phase data-sharing project designed to improve clinical decision making, includes AACR and seven institutions in genomic sequencing.

• **ORIEN, the Oncology Research Information Exchange Network,** founded by Moffitt Cancer Center

and The Ohio State Comprehensive Cancer Center. ORIEN is a self-governed alliance of NCI-designated cancer centers built around a standard consenting and processing protocol called Total Cancer Care (The Cancer Letter, March 13, 2015).

Unlike GDC, other initiatives primarily limit their data to somatic genetic changes and mutations, Staudt said.

"They may not know whether a mutation was in the germline, and often won't have precise information about the quality of the data that underlies the determination that there is a mutation," Staudt said. "One of the benefits of keeping the raw data is that we will be able to implement better and better algorithms and tools in bioinformatics as they are being developed.

"So when the other groups are sharing the data, what they are doing is sharing very derived data that is divorced from the actual data," Staudt said. "The GDC is doing something different.

"We enable researchers to embark on a perpetual cycle of improvement and reanalysis of data, ever increasing in precision and scale. Other projects, at least as currently defined, will only include the results of analyses, and in many cases, we won't be able to say whether a particular algorithm that was used might have missed something, or incorrectly called a mutation. That is not trying to denigrate what others are doing—what they're doing has real value—but I'm just trying to distinguish what we're doing.

"That said, we're excited about all efforts to discover important associations between variants and clinical responses and would like to offer the GDC as a useful and permanent venue to share the data."

Major players in cancer informatics should collaborate, share data and create common standards, Niland said.

"It would be great to bring all these initiatives together," said Niland. "City of Hope is sharing data with ORIEN, which is matching the clinical data with the tissue data and the genomics that result from the molecular profiling and having the whole package.

"I think ORIEN could contribute to the moonshot as could the GDC, but we all need to come together and use common standards. We need to interoperate and share and integrate across the initiatives, have one contribute to the other. Down the road, that would be ideal.

"We shouldn't be saying, 'Oh there are so many standards, I don't know which one to choose.' There should be one standard, although this is very difficult to achieve.

"The GDC has a very impressive advisory group here, I hope they would reach out to other initiatives and come to a consensus internationally."

How the GDC Works

The GDC splits its data into two categories: controlled access and open access.

The open access data includes mutations discovered in TCGA that are in protein coding regions of the genome and were deemed to be somatically acquired, i.e. only in the tumor, not in the germline of the patient.

Controlled access data can only be used by qualified academic researchers, who have to apply for access through the dbGaP—the NCBI's database of Genotypes and Phenotypes. These investigators are required to provide a research plan, abide by a data use agreement, and agree not to redistribute or violate the privacy aspects of the data.

"We have already implemented a browser that has a very menu-driven, clickable way to choose cases based on the stage of disease or anatomical location, age of the patient or a variety of other clinical characteristics," said Staudt. "Or you will be able to do it the other way around: you can say, 'Show me all the cases that have mutant KRAS and their associated clinical characteristics.'

"We are implementing three mutation callers in the GDC. The majority of the mutations are called equivalently by all three algorithms, but on the edges, each one of them will call some other mutations that are actually real and missed by the other callers.

"We have already implemented two mutation-calling pipelines and are close to finishing the third pipeline, and each of them takes quite a lot of time—weeks—to finish processing all the data."

The GDC will be functional by the June 1 launch, but NCI will continue to add features on a monthly basis.

"We will start the process of accepting outside data on June 1, but I don't think we'll be able to get the first data in for a month or two," Staudt said. "It will take us that amount of time to figure out exactly how to get it in so it's fully correct.

"There were things that we thought about that seemed too difficult to put into the GDC at the very beginning and so they're not there, and they will be coming in after June 1. The GDC will continue to improve at a fairly rapid pace over the two years following its opening in June—it will keep on improving even after that."

Interoperability and Past Lessons

The GDC is built to be interoperable, Staudt said.

"We've been envisioning that we want to interoperate with other systems as much as possible," Staudt said. "It was a condition of the contract that the GDC should maintain awareness of international standards and interoperate to the extent warranted.

The devil is in the details, because it's the annotations and data identifiers that matter the most, Kibbe said.

"What's really changed in the computer science world is the data structures you pick are less important than the identifiers. Every data item in GDC has a rich collection of metadata around it," Kibbe said. "The ability to add new identifiers around a data element completely changes how you can interoperate between different systems."

That level of granularity is the only way to deal with the complexity of relationships within the data: from a patient to the treatment and the tumor sample, as well as five different types of analysis that is performed on each DNA and RNA.

"What it means is that every data element is a separate file and object on the computer, so that there's no traditional relational database, so to speak," Staudt said. "Everything object can be directly related with all the others since, as Warren said, you know exactly what each object is by virtue of its metadata."

The biggest challenge in oncology bioinformatics is annotating phenotypic and clinical data as rigorously as genomic data, Niland said.

"My background is primarily in clinical research and I realized that you can't do as much as you'd like to do with genomic data without that phenotypic and clinical data," Niland said. "You can't make sense of a person's genomic information if you don't know exactly what disease they had, what stage, what comorbidities they had, what treatments they received, and what the outcomes were.

"If you really want to interpret the data and find patterns and associations and adjust for covariates and all that, clinical outcomes data etc. needs to be as rich and as standardized as possible. I think that's the biggest challenge for the moonshot."

Staudt and Kibbe said that NCI has learned valuable lessons from caBIG.

Launched about 14 years ago, the $350 million bioinformatics venture went beyond its original mission of making it easier for cancer researchers to exchange data and attempted to fulfill two clashing missions: (1) setting the standards for computer tools and (2) promulgating tools that meet those standards.

In 2011, an NCI Board of Scientific Advisors working group found that conflicts of interest—intellectual and organizational—afflicted the ambitious project.

NCI officials said the caBIG fiasco taught the institute to limit its goals and use of resources to solid deliverables and timelines.

"Before we even put out the contract announcement for this, we spent nine months of regular weekly meetings working on developing a statement of work for the GDC," Staudt said. "We really specified exactly what we wanted the GDC to accomplish. The GDC development team knows this is a contract and not a grant. We said, 'This is what you're going to deliver,' and they're delivering it.

"The big thing is that we didn't try to do everything you can do in informatics. We had a very well delineated task in front of us, and we figured out a plan to accomplish it. Bite off what you can chew."

The teams overseeing and reviewing the GDC project are:

GDC Steering Committee Members

Stephen Chanock, of the NCI Division of Cancer Epidemiology and Genetics
Li Ding, of the Washington University at St. Louis
Gaddy Getz, of the Broad Institute at MIT
David Haussler, of the University of California Santa Cruz
Warren Kibbe, of the NCI Center for Biomedical Informatics and Information Technology
Chris Sander, of Memorial Sloan Kettering Cancer Center
Ilya Shmulevich, of the Institute for Systems Biology
Louis Staudt, of the NCI Center for Cancer Genomics
John Weinstein, of MD Anderson Cancer Center
Barbara Wold, of Caltech
Jinghui Zhang, of the St. Jude Children's Research Hospital

Bioinformatics Advisory Group Members

Barbara Wold, of Caltech
Gad Getz, of the Broad Institute at MIT
David Haussler, of UC Santa Cruz
Chris Sander, of Memorial Sloan Kettering
Ilya Shmulevich, of the Institute of System Biology
Josh Stuart, of UC Santa Cruz

Subject Matter Experts

Sheila Reynolds, of the Institute of System Biology
Jing Zhu, of UC Santa Cruz
Kyle Ellrott, of Oregon Health and Science University
Gordon Saksena, of the Broad Institute at MIT
Ivo Gut, of the Centre Nacional D'analisi Genomica in Barcelona, Spain
Angela Brooks, of UC Santa Cruz
William Lee, of Memorial Sloan Kettering
Katherine Hoadley, of the University of North Carolina

Conversation with The Cancer Letter

Staudt and Kibbe: Commons Will Publish Raw Genomic Data

(Continued from page 1)

"When the other groups are sharing the data, what they are doing is sharing very derived data that is divorced from the actual data," said Louis Staudt, director of NCI's Center for Cancer Genomics. "The GDC is doing something different.

Staudt and Warren Kibbe, NCI acting deputy director and director of the NCI Center for Biomedical Informatics and Information Technology, spoke with Matthew Ong, a reporter at The Cancer Letter.

Matthew Ong: *When did the idea for the Genomic Data Commons come about and what drove the need for NCI to establish the GDC?*

Louis Staudt: That was on my watch. I was asked by Harold Varmus to take over the Center for Cancer Genomics and be its first permanent director. I started learning about what I was suddenly in charge of, which was The Cancer Genome Atlas program, and the great raft of data that was being generated and how it was served up to folks.

Traditionally, this kind of data would be maintained by the National Center for Biotechnology Information, which is one of the centers here at NIH. But the size of this is so large, the amount of data so great, that it exceeded their actual limit, they basically didn't have the ability to take this on.

The other thing that was very clear, when I started learning about how the TCGA operated, was that it was very quickly and effectively prosecuted as a project, and because of that quickness, it was happening in multiple centers in parallel often using similar, but not identical technologies and the data were analyzed in similar but yet not identical ways.

Still, we made a lot of progress in the TCGA project, even given those imperfections. But it seemed like we could do a better job of analyzing and presenting the data. We also needed a long term place for the data because, of course, the National Cancer Institute, as the steward of our public resources, needed to make the data available for as long as it's still relevant, which is probably going to be a long time.

And what's more, we need to keep the data freely available, so that cancer researchers can get at it. Public access to TCGA data has paid off in spades because there have been over 1,000 papers published based on the data.

So we had to do something with the data. The data was outstripping the mechanisms we had put together for storing it. I felt that it was necessary to tackle this in a very concerted fashion, working with the best computer scientists to implement uniform, state-of-the-art bioinformatics protocols and generate what we call "harmonized" data. In this way, all the data from the TCGA and from any other genomics project that we would do would be all analyzable in a common framework.

That was the genesis of the GDC. The initial groundwork was probably late 2013, when we were starting to draw up the plans. The other thing that was very exciting at the time, and remains so, is if we made a bioinformatics engine and made all that software available to cancer researchers, could they then start uploading their own data that they have generated? And the carrot would be that they get to use all of the wonderful software that had been constructed during the TCGA project and get the best possible analysis of their data. The stick would be they must share the data, and they must share it openly and publicly. So that's the second piece that we really didn't have before.

When we open this up for business in June of this year, we will start taking in projects from anyone in the world who has done a well-annotated cancer project that would add value to the whole.

The final thought—quite aspirational and not realistic at the moment, but exciting nonetheless—is based on the fact that we are moving towards more routine genomics for patients diagnosed with cancer, in the course of their care. If that ends up being the case and there is funding to pay for that, then what would it look like if individual cancer patients started donating their cancer genome sequence to this public repository? Then, suddenly, we'd be getting hundreds of thousands of datasets that we didn't have to fund centrally. But given the great diversity that is the essence of human

cancer, one needs to get data from over 100,000 cases to have sufficient statistical power to discover all the recurrent genetic driver events that cause cancer.

I just want to be clear, this has not been implemented yet, and there are some barriers to implementation, but it's kind of fun to think about.

MO: *So you're saying that when the GDC is launched, nearly anyone in the world—not just NCI-designated cancer centers—can mine data as well as contribute data, right?*

LS: Yes, the GDC will be openly available. For data submission, we will look at the quality of the data and whether it's a large enough dataset to make a difference, because everything takes time and we're going to have to help investigators get their data in order. But yes, any sort of well conducted study that you are writing a paper about, and you have molecular data and hopefully some clinical outcome data or some sort of clinical data, is potentially appropriate for the GDC, meaning that you can use the GDC tools as long as you agree to share your data.

In the TCGA and the other projects NCI has conducted, we have collected clinical data in a very elaborate and fine-grained fashion. Keeping that all straight and serving it up in a way that is easily searchable so that you can find the cases that you are most interested in is a bit of computer science that took some work to get right.

The GDC will store the genomic sequences along with the analysis of the tumors, and also store the enrollment clinical data and treatment data for these patients. The overarching goal is to move towards a knowledge base for cancer, which will develop a clinically useful molecular taxonomy of cancer that will help us evaluate for any particular patient what the most rational course of action is.

MO: *What are the incentives for hospitals and cancer centers to come to the NCI and say "Hey, we've got really valuable data and we want to put that into the GDC and make it publically available." What incentives would drive people to want to do that?*

LS: There are probably many. One very practical incentive is that if researchers would like to publish a paper in most good journals nowadays, they must make their data available according to the journal requirements, and typically that is in a public database like the GDC.

Secondly, again in the realm of research, if your data were collected using NIH funds, then we have a new policy called the NIH Genomic Data Sharing Policy that went into effect January of last year [see https://gds.nih.gov and http://www.cancer.gov/grants-training/grants-management/nci-policies/genomic-data]. That says, in no uncertain terms, that you must share genomic data and associated experimental data.

The GDS stipulates that you must consent the patients on your study for the analysis of their samples so that their data can be shared in a controlled access environment. You must follow through on that. And we will probably figure out ways of enforcing that and making sure that people are living up to that policy.

And the final point is that there is an altruistic streak that is gaining momentum, which I have certainly embraced from the early days of genomics. When you generate this very high-dimensional data, and you write a paper telling the world about the most interesting thing you found, you know that you haven't described all of it and that someone else may have a different perspective. Sharing the data broadly will inevitably lead to more knowledge generation.

I've often used other people's datasets in my own research. I didn't have to do anything, all I had to do is click a button and the data was on my computer. And that has been very useful in making my own data richer, allowing me to interpret it better. I think that publically funded data should be made publicly available. Data from tumors and cancer patients is critical to solving problems in cancer, which is what we're all about. We're hearing this perspective from many corners, including AACR and ASCO, and NCI is trying to be a leader in data sharing—certainly that's been loud and clear in many discussions about the moonshot.

Warren Kibbe: From a position standpoint, what we'd really like to see is all the groups that are out there collecting these kinds of data, that they actually have a place available to them to share it. And along with genomic data, they need to be able to share all the clinical information, the phenotype around the genomic information, in a way that is well-described, well-defined, and accessible for data sharing as well. I think the GDC is a great platform for people to do data sharing and that's really what it's designed to enable.

MO: One of Vice President Joe Biden's goals for the National Cancer Moonshot Program is breaking down data silos and establishing a central data repository. I know that many are hoping to be that central repository. In that context, what role do you see the GDC playing in the moonshot program and how will it achieve that goal?

LS: We're really happy that other groups are trying to do this and working through some of the impediments that naturally come up with the sharing of data. I think

that, ultimately, if they come up with a way that they're going to share their data, then I guess they can share it with the GDC and we can help distribute it. The one thing I think is a little special about the GDC is that there will be only one such NCI-supported system. That doesn't mean there won't be a lot of other activities, some of which Warren is coordinating—that will be computational genomics to help understand what all the data means.

But, as a data repository, it's unlikely we'll be able to fund a large number of long-term, large data repositories. So I think that the permanency that is inherent in what we're trying to achieve in the GDC would be seen as a real benefit to anyone who's trying to share data.

So I applaud them for doing it, working through the problems, making discoveries, and publishing them. We'd like the GDC to help maintain the data and make it continuously available.

MO: *At a roundtable at Duke, Biden expressed his astonishment at the number of duplicative efforts in oncology bioinformatics. How is the GDC different from others?*

LS: There are certainly many exciting bioinformatics approaches to find drivers for cancer and display the data. However, the GDC is unique in many ways, and I'll tell you an important one. We are keeping all the raw data and we keep it in a controlled access way that allows researchers who have the permissions and acumen to look at it. What these other projects are doing—full disclosure, I'm on the external advisory committee of the GENIE Project, so I know about that project and I know also about the others—is that they are going to try to share the somatic genetic changes in the tumor. They may not know whether a mutation was in the germline and often won't have precise information about the quality of the data that underlies the determination that there is a mutation. One of the things about keeping the raw data is that better and better algorithms and tools in bioinformatics are being developed rapidly. Based on the type of data that comes off of our high-throughput sequencers, it's not also clear whether or not there is a mutation, but having the raw data will allow us to implement uniform, well-defined analytical pipelines to make the best determination possible.

Largely, the difficulty arises from the incredible complexity of human cancers. Some mutations are only in a minority of the cells within the tumor—let's say 2 percent or 5 percent of all the tumor cells have a particular mutation. At this frequency, the real data are approaching the noise in the system, so we have to solve a signal vs. noise problem.

So when the other groups are sharing the data, what they are typically doing is sharing very derived data that is divorced from the actual data. The GDC is doing something different. We enable researchers to embark on a perpetual cycle of improvement and reanalysis of data, ever increasing in precision and scale. Other projects, at least as currently defined, will only include the results of analyses, and in many cases, we won't be able to say whether a particular algorithm that was used might have missed something, or incorrectly called a mutation. That is not trying to denigrate what others are doing—what they're doing has real value—but I'm just trying to distinguish what we're doing.

That said, we're excited about all efforts to discover important associations between variants and clinical responses and would like to offer the GDC as a useful and permanent venue to share the data.

MO: *What is the status of conversations between NCI and the vice president's office, as well as the other bioinformatics groups? What responses have you been receiving from both of those parties?*

LS: Everybody likes the GDC. I certainly know that our director, Doug Lowy, has mentioned the GDC on a number of occasions. It is clear that the GDC is going to be part of the solution.

WK: When we've been talking about the GDC and the cloud pilots, and both of those come up with the vice president's office, they're very interested in how we can really use what we've been developing to push the cancer data sharing agenda.

What the vice president's been saying is we need to make these data available, and discoverable, and we need to learn from all the data that's been generated across the country. I think that the way we've tried to describe the GDC, relative to all the rest of the projects and initiatives that are out there, is, as Lou said, that the GDC has the raw data. Another advantage for the GDC is consistency—all the genomic data that gets submitted to the GDC is run through a consistent analysis pipeline.

Because we get the raw data, we also make sure that it passes a certain QC threshold, and that when it doesn't, we can annotate that as well. Again, there's a piece of what the GDC brings to the table that is distinct from, for instance, trying to aggregate all the genomic data or all the panel sequencing data from every hospital in the country.

LS: Although the special sauce of the GDC is

having the raw data, if someone wanted to drop, say, 10,000 cases on us with tumor resequencing and just provide the somatic mutation calls, we will gladly make that available and searchable, and use all the tools of the GDC to be able to look at that data in the context of all other GDC data.

The one thing that I think we need to emphasize is that the data that are generated at these centers largely are resequencing data, looking for mutations—typically, that's all they're looking for. That is not sufficient to fully describe the molecular nature of a cancer. At a minimum, you also need to describe the activity of the genes as read out by the messenger RNA levels, which gives you part of the phenotype of the cancer cell, as well as chromosomal copy number changes - too many copies of a gene or deletion of a gene—and rearrangements of a gene.

Largely, the panel sequencing that's being done routinely at the centers is not looking at that sort of multi-modality data, and it's only by embracing all those data dimensions that we are going to provide a full molecular picture of a tumor, which will be important for patients. It's not only, "Yes, you have a mutation in a gene for a particular pathway that may make this cancer susceptible to a drug." If you have high-level amplification or high expression of a gene in the same pathway, that tumor can be just as addicted to that signaling and just as killed by that particular drug.

It's this multi-platform integrative analysis that is also a special aspect of the GDC.

MO: *Warren, you mentioned that the vice president is excited about the GDC, do you know the VP's office has indicated or in any way said, "The GDC looks like our solution"?*

WK: Well, we'd love it if that were true. I'm not sure that the vice president himself has heard about the GDC. We've certainly given that information to the vice president's office.

Also, in the GDC, it's not just the pipeline for analyzing all the data, it's also how you can find it and visualize it. There are actually a lot of tools that are available to help people make sense of the data they are generating. You asked what's the secret sauce for getting people to share their data—one part of that, of course, is the Genomic Data Sharing Policy.

If you get NIH funding for generating cancer genomics data, there is an expectation and a requirement that you share those data. When the GDC opens, the requirement will be that for NCI-funded investigators generating genomic data, the data has to go to the GDC.

But, just as important—and this is the carrot side of it—you get access to this incredibly well defined computational infrastructure that has all the computer science behind it that we currently understand and have vetted for analyzing genomics.

That's a tremendous value for the community, and we'll see how that plays out. We've been getting a tremendous amount of interest from a number of projects—can they deposit their data in the GDC to make it available to the community? That's exactly what it's there for.

MO: *What is the timeline? When will people be able to see the GDC?*

LS: It's going to open up on June 1 of this year. We're hoping that we can withstand the surge, and we feel the usual fear and trepidation that goes into opening up a big data system. Something that I've appreciated is how complicated this has been from a computer science point of view, but the team is doing a great job and we're doing lots of user testing with interested parties, so it won't be just an untested system when it opens up.

Then, what will be relatively untested and involve some growing pains is to learn what it means to take in other people's data. The only difficulty there is we don't really know what the data will look like. By definition, everybody could be using a different data provider, and the data will be formatted in different ways. We've been working hard at generating controlled vocabularies of how the data must be submitted, but there's going to be some handholding—that's going to be part and parcel of what we will need to do to get the data in.

So we will start the process of accepting outside data on June 1, but I don't think we'll be able to get the first data in for a month or two. It will take us that amount of time to figure out exactly how to get it in so it's fully correct.

WK: It will also depend on how big those projects are, which will influence how long it will take to get the data into GDC. With TCGA itself, just getting a petabyte or so data over a 10-gigabit line took several months. While I don't think there are a whole lot of projects that size that are out there waiting to deposit data in the GDC, there can be a delay in getting the data in. It's not something that happens overnight where you flip the switch and suddenly there's a whole big dataset there.

Actually, a lot of work goes into importing the data and resolving all those ambiguities in the data. There are always far more questions about the data than it seems like there ever should be, considering that it's all generated with machines, but it's there, it's real,

and it does take people paying attention to fix all of it.

MO: *Is caBIG relevant to the GDC? Are there any lessons to apply here?*

LS: It's very relevant. Bite off what you can chew. Before we even put out the contract announcement for this, we spent nine months of regular weekly meetings working on developing a statement of work for the GDC. We really specified exactly what we wanted the GDC to accomplish. The GDC development team knows this is a contract and not a grant. We said, "This is what you're going to deliver," and they're delivering it.

There were things that we thought about that seemed too difficult to put into the GDC at the very beginning and so they're not there, and they will be coming in after June 1. The GDC will continue to develop at a fairly rapid pace over the two years following its opening in June—it will keep improving even after that.

So it was important to think a lot about the scope of what could be accomplished and the resources it would take to do that, and hold ourselves accountable for deliverables along timelines that were realistic but would get the product out in a time that is appropriate for the need. That is, we didn't want to take more than two years to get something done that was useful, and that's exactly what the GDC team has had—two years.

By the way, the GDC team has been doing an absolutely great job. GDC development is led by Bob Grossman at the University of Chicago [director of the GDC project, chief research informatics officer in the Biological Sciences Division, and professor of medicine at the University of Chicago], with very valuable contributions to the front end user interface by a team at the Ontario Institute for Cancer Research. We also have a really excellent team at our main NCI contractor, Leidos, who has been managing the GDC development along with all of us at NCI. It's been team science putting this all together.

The big thing is that we didn't try to do everything you can do in informatics. We had a very well delineated task in front of us, and we figured out a plan to accomplish it.

WK: The only thing I would add that is crucial and is basic to what Lou does—it's second nature—is the engagement of the whole research community in this. He was talking about TCGA; TCGA investigators have been really involved in helping to specify what the GDC needs to look like, as have the TARGET teams.

So what's been phenomenal is that TCGA started as a relatively insular project—nobody really knew how it was going to turn out—but by now, eight years later, it involves a huge community of researchers. They really rely on the TCGA data for many things; they've also contributed to it in fundamental ways. That's not just the folks that have grants and contracts around TCGA, it really is the whole genomics and cancer research community.

That involvement of everyone really makes this project much better, and of course, it's hard to manage all of that, and Lou's group really does a tremendous job managing the different stakeholders and making sure what is going into the GDC meets the community's needs. That's a really important lesson.

LS: Warren's right—that's a lesson learned from TCGA as well as how I do business in general. Team science is something that should be embraced and probably a bit of a contrast with the past.

MO: *Can you go into more detail the GDC's arrangement with the University of Chicago and OICR through Leidos? How are they uniquely qualified to develop and manage the GDC?*

LS: Good questions. First of all, this was a competitive process, as it always must be. We got quite a few good applications, and the Univ. of Chicago proposal was deemed by an outside panel to be the best from a number of perspectives. Bob Grossman himself is a national leader in big data and has brought a lot of expertise.

The actual computer science construction of the GDC is unlike any database that's held cancer genomics before. It's not a standard, typical relational database from Oracle, it's a different, modern version. It allows much more flexibility in dealing with these data that have many connections that need to be maintained with one another. So Bob has brought that approach from his computer science background.

The way it works is this: Leidos is our contractor, and they subcontract the work out to the University of Chicago, the primary subcontractor. OICR has been doing a lot of the informatics for the International Cancer Genome Consortium, especially the front end website for browsing the ICGC cancer genomics data. Bob naturally turned to them as a sub-subcontractor for the project to bring in that web development.

OCIR has been working with the University of Chicago team to optimize very complicated queries of the enormous amount of data in GDC, so that, even if it's not instantaneous, you're not going to wait too long for an answer. That's computer science. We needed somebody bringing that to the GDC, with an emphasis on the science part of it.

Some time was spent testing out systems that were purported to be good and then when we tried to deploy them on the petabyte scale, they failed miserably. So we said, "Okay, scrap that, we've got to go to a different system." So there's been a learning curve during the development of the GDC. That, in a nutshell, is an example of how the team has been doing a great job.

Leidos is obviously critical to a lot of what we do here at NCI. They allow us to develop projects that must necessarily occur over a period of time—this mechanism is ideal for longer-term projects like the GDC, with its initial phase of two years, followed by option years in which the GDC is improved and extended.

I want to commend the actual leads at Leidos that we brought in to help manage it. Developing a complex computer system requires active management: What's done now? What's done later? Where are we currently? Are we behind on this task? What priority is most pressing now? The Leidos team has been very important in doing that and has been instrumental to the success.

MO: *What is the budget for the GDC for the 2016 fiscal year? Is it funded through the CCG?*

LS: I can tell you what it has been. Through the two-year period, it's been $20 million, and we're just working on the budget for the out years at the moment.

MO: *What progress has the GDC made since the initial announcement in December 2014? Where is the project now?*

LS: We've made a lot of progress. As Warren mentioned, the data are enormous. Just to get the data in from where it's currently sitting took months, and there's the added complexity of fixing certain aspects of data that weren't quite right. That took a long time. The second big task was mapping the sequencing data to the genome. As you know, with high-throughput sequencing, you get millions upon millions of short DNA sequences from each cancer and from the normal DNA of the same patient. Each of these sequences needs to be placed by an algorithm somewhere in the genome, which a pretty big territory—it's 3 billion base pairs.

Even to analyze one sample, it takes hours to a day, so the team at Chicago figured out a way parallelize that process, allowing them to process data from roughly 11,000 cases from the TCGA, another 1,000 to 2,000 pediatric cases from TARGET, and a smattering of 500 or so cases from various other projects. The genome mapping of all of these data has been successfully completed over several months.

By the way, all of the software is becoming standardized—the official term, I learned, is dockerized—which means to a computer scientist that they can just take that code and implement it readily on their computer, and it will work. That's remarkable, because usually a computer system is highly tied to the particular architecture of the operating system. So all of these methods that we've developed to do this big data analysis are themselves publicly available and reusable by the community.

One other basic task, that was not at all trivial, was to get all of the very complicated clinical data from our various cancer projects in order and searchable. That was a big curation effort.

The next question is, "Alright, what's there? What are the genetic abnormalities?" You would think that would be easy, but in fact the science on that is still progressing, and we determined that, at present, there's no one right answer to whether or not there is a mutation in a cancer. We're implementing three different mutation callers, all respected, all have their pluses and minuses, and we will make all of them available to the users of the data—that's also something that's unique to the GDC.

I don't want to make you feel it's all a mess: the majority of the mutations are called equivalently by all three callers, but on the edges, each one of them will call some other mutations that are actually real and missed by the other callers. As I mentioned earlier, this is due to the complexity of human cancers. A tumor biopsy does not only contain the malignant cells - there are infiltrating immune cells and other cells that dilute the mutational signal from the malignant cells. Secondly, tumors can have minor subclones that differ genetically from the major clone, but the mutations in the subclones are only found in a very low percentage of the sequencing reads. This percentage can approach the error rate of high-throughput sequencing, so you can be confounded by experimental noise. We have implemented two mutation calling pipelines and are close to finishing the third pipeline, and each of them takes quite a lot of time, weeks, to finish processing all the data.

The final big task is to make what we hope will be a really useful, attractive browser for the data that will allow you to identify cases by their clinical attributes or molecular features, and focus your analysis of those cases, and download the data to your computer for future analysis if needed. That frontend browsing interface has taken a lot of effort to get right. Equally challenging has been our efforts to optimize the experience of people trying to upload data to the GDC.

They have to get their data formatted correctly. How can we make that easier for them to do? That's been a big part of our work.

It looks like we're on track to meet our goal, our deadline. This is a work in progress—even after GDC opens, we're going to be adding features on a monthly basis. Nonetheless, we'll have a lot of functionality when it opens.

MO: *Since many of our readers consist of faculty at academic cancer centers, could you explain who has access to the data? How accessible and easily usable will the data be? Also, how will NCI maintain the quality of the data?*

LS: There are two types of data, controlled access data and open access data, and the type of data differs by each project and depends on how the consent for the patients was set up. In the TCGA project, those mutations that are in the protein-coding segments of the genome and are deemed to be somatically acquired—not in the germline of that patient but only in the tumor—are open access. This means that they will be available to anybody, and GDC will provide browsing tools to help people see where they are in genes, and what types of tumors have which types of mutations.

The second type of access is for controlled access data, which means that you apply for access through the standard NIH mechanism, which is the dbGaP system. For this you typically have to be a qualified scientist at a research institution, provide a plan of what you would like to do with the data, abide by a data use agreement that has been established for the project, and agree, for example, not to redistribute the data on the Internet or do anything else that would violate the privacy restrictions attached to the data. Then, once you have dbGaP approval, you can work with the controlled access data in GDC.

In terms of the GDC experience for the cancer researchers, we hope GDC will be useful when we launch and steadily improve over time. We have already implemented a browser that has a very menu-driven, clickable way to choose cases based on the stage of disease or anatomical location, age of the patient or a variety of other clinical characteristics. Or you can do it the other way around: you can say: "Show me all the cases that have mutant KRAS and their associated clinical characteristics."

There will be some browsing functionality at the get-go. You will be able to find data, download it, and visualize it to an extent, but advanced visualization tools take time to develop and will be continuing to improve over the next two years.

By the way, we will entertain all sorts of improvements from the community and take suggestions for tools that might belong in the GDC. Warren is in charge of another big project, called the NCI Cancer Genomics Cloud Pilots, which is developing a bunch of tools to work on these data. If some of them look really useful and give us a new view of the data, then we'll just make them an integral part of the GDC.

MO: *Does NCI have any plans right now to interface with other databases? What is NCI's approach to interoperability, and will the GDC be interoperable?*

LS: We've been envisioning that we want the GDC to interoperate with other systems as much as possible. It was a condition of the contract that the GDC should maintain awareness of international standards and interoperate to the extent warranted. There is an international group of investigators called the GA4GH—the Global Alliance for Genomics and Health—who have been thinking a lot about how to develop standards for accessing genomic data. Given the complexity of setting standards on a global scale, there is a real appreciation that what we're developing in the GDC might help drive the conversation in GA4GH as much as anything else.

Right now, there's not a standard coming from the GA4GH for a lot of the types of data that we're implementing in the GDC, and we think that some of what we have developed will be useful for generating those global standards. We're not alone in wanting to analyze cancer genomic data: many other countries have made big contributions in this area, and therefore, we need a way to interoperate with them.

For a variety of reasons, it is somewhat unlikely that there will be one large international database of cancer genomics—I think there are some impediments that are difficult to get around—but a virtual way of accomplishing the same goal is something that a lot of people are envisioning. For researchers who have access privileges to data in several repositories, it may be possible for them to send computer programs to the location of data, derive results, and bring them into a common workspace. We would be very interested in helping to support that kind of global sharing of the data.

MO: *It seems like a lot of discussion in oncology bioinformatics is moving towards creating a common set of standards for good curation of data. Will GDC become a gold standard for genomics data?*

LS: I think that's a little strong. We will lead by example, and endeavor to make useful tools, all of which will be open source and hopefully easy to

implement. If our tools are good, then people will adopt them, and if someone comes up with a radically better tool, we will adopt it and make the GDC better. But, we do hope that we have been at the leading edge of development of informatics for cancer genomics, and that some of what we have done will drive the conversation.

Other groups are doing things that we're not doing. For example, the ASCO system concerns data from clinical practice and that's quite different from what we're going after here.

WK: I think what has changed is that the data structure isn't the big deal. It's actually how you attach metadata identifiers to the data so you can really tell what it is, what the particular data element is. What's really changed in the computer science world is the data structures you pick are less important than the identifiers.

That's something that's important as we try to build interfaces with data from other groups—they'll be able to expose their data with identifiers, enabling interoperability. True interoperability has been really hard to achieve in the clinical setting but it really seems like we're on the verge of being able to do that in cancer genomics.

The GDC, as it's being built, should enable people to explore the data in many different ways and discover what's inside the GDC, or contribute to it. Every data item in GDC has a rich collection of metadata around it. The ability to add new identifiers around a data element completely changes how you can interoperate between different systems.

The GDC is built in a very different way than anything that NCI's ever built before and is very different from most cancer genomic systems that are still being built. It is being built on big data principles, meaning that there's enormous flexibility in being able to take in different kinds of data and have them interoperate with each other.

LS: What it means is that every data element is a separate file and object on the computer, so that there's no traditional relational database. Everything object can be directly related with all the others since, as Warren said, you know exactly what each object is by virtue of its metadata. This is the only way that you can deal with the complexity of relationships among GDC data elements. This open data structure allows us, for example, to relate a patient to a treatment regimen, to biopsy samples that came from the patient, to DNA or RNA preparations that came those samples, and to the several different types of genomic analyses that were performed using that DNA and RNA.

Just by that one sentence you can see how complex the relationships can be within cancer genomics data. The modern data structure that is implemented in the GDC is the only way to deal effectively with these relationships at the scale of two petabytes of data. In other words, you will not have to come back after lunch to get the answer to your GDC data query.

MO: *Since this is going to be a permanent database for the long term, where do you see the GDC five, 10, or even 15 years from now? What do you envision this to be?*

LS: I think the really cool part is to transform the GDC into an actual knowledge system in which we incorporate not only the raw data from patients' tumors, but also information that's relevant for interpreting the functional importance and clinical relevance of the genetic changes in the tumors. I'll just focus on mutations for simplicity, but the same could go to a lot of other molecular abnormalities. Some mutations are important for the cancer process and contribute to malignancy. These mutations are called drivers. There are a lot of additional mutations in a tumor that are actually just along for the ride and do not contribute to malignancy—they're called passengers.

We're at a very rudimentary stage of distinguishing these two types of mutation. Currently, there's a bit of a growth industry among cancer researchers that entails the testing of mutations identified in large scale projects like TCGA in a variety of different functional assays in order to help determine which ones are drivers and which are passengers. We can put all of that information into the GDC and use it to annotate the genetic data from tumors.

A second major goal is to accrue cases into the GDC that have better clinical outcome data, allowing more informative associations with genomic features. In the TCGA project and in TARGET the primary goal was to perform genomic analysis of a large number of tumors in order to describe the genetic landscape of cancer. A secondary goal in these projects was to get clinical data.

Typically these data were not collected in a controlled fashion, as would happen in a clinical trial, and the length of follow-up following treatment was not as long as you would like. For this reason, we're initiating a number of new projects in the NCI Center for Cancer Genomics to perform genomic profiling of tumors from several NCI-sponsored clinical trials. Many of these trials have completely accrued and have mature outcome data, allowing us to ask important questions

about which molecular alterations cause tumors respond well or poorly to particular types of therapy.

By implementing multi-modality genomic characterization and capturing pristine clinical data from the clinical trials, we're hoping to identify the genetic lesions that dictate response or resistance to treatment, thereby fostering precision oncology.

Very aspirationally, we imagine that the GDC could be used as a reference system for the molecular diagnosis of cancer in a way that influences the care of individual cancer patients. Developing the necessary knowledge base for this will be the focus of research for many years, requiring much more data regarding the relationship between genomic alterations and treatment response. In the future, we imagine that clinical tests could use GDC data and methods to recommend a course of treatment for a patient. Of course, such tests would have to be performed in an appropriate clinical laboratory environment, with approval by regulatory agencies like the FDA.

That's why we're making the GDC—to change, for the better, how patients get through their problem with cancer.

Guest Editorial

Boyle on the Moonshot: A Personal, European View

(Continued from page 1)

President Barack Obama reiterated this development in his State of the Union address announcing a new national effort to get it done and placing Vice President Biden as leader of this initiative.

The appointment of Vice President Biden to head the initiative is an inspired choice.

Of course, let's not forget that in 1971 President Richard Nixon launched a not dissimilar initiative and yet 45 years later, there still remains an on-going war against this feared group of diseases, despite progress in many aspects. Times change, knowledge advances, and there are many signs that this new initiative holds out a better chance of *success*.

To emphasize the seriousness of this Moonshot, one of the initial moves was to convene a meeting of the White House Moonshot Task Force involving the heads of relevant executive branch departments, agencies, and offices. Vice President Biden emphasized that it would take a whole-of-government approach to help achieve the goal of the moonshot--to make a decade of advancements in the next five years.

The entire federal government is engaged.

Detailed plans have emerged slowly, but the address delivered by Vice President Biden at the recent meeting of the American Association for Cancer Research, captured in a recent edition of The Cancer Letter, was quite informative.

Last year, the 2016 budget funding for the National Institutes of Health was increased by $2 billion, the largest increase in a decade, and he added that the White House is requesting another $800 million to support research activities across multiple federal departments as part of the anticancer effort.

Biden provided another focus—other than 'cure'—during this speech emphasizing the initiative's goal to advance research more efficiently and more rapidly. He noted that President Obama had signed essentially what is an executive order giving him control over all the federal agencies and departments, from Veterans Affairs to the Department of Energy, to engage whatever resources necessary to achieve the Moonshot goals.

The coordination across a wide variety of government departments is a quite remarkable development in the history of research. It says very clearly that this is a very serious endeavor with whatever federal resources considered necessary to be engaged on the Moonshot.

In addition, the convening power of the Office of the Vice President in bringing together what are often politically and culturally entrenched research interests to put aside their differences and focus on what matters, the patient, is remarkable.

Biden launched a consultation for recommendations and has announced that the Task Force has received several including increasing research budgets across the Federal government; making it easier to share data; removing paywalls around published research; and incentivizing verification of study results.

Viewing the evolution of this Moonshot from Europe, there is much to be admired and much that we can learn.

Among other issues, Biden emphasized the need to close the time gap between submission of a research grant and the announcement of the outcome. This would be a valuable lesson that should be learned in Europe.

The amount of time scientists spend writing grants, often with copious detail as a requirement, is dispiriting and the long gap between submission and outcome is a major impediment to progress in science.

Three cheers for Biden changing this and there will be the same when the European Commission and many

national research funding organisations follows suit.

Sharing research data is an issue which has been much debated. In principle, it is a great idea, but there are pragmatic hurdles to overcome. It is clear that data sharing could become a condition when receiving federal funding. How can recipients of grants from other non-federal sources be forced to make data available for sharing?

Perhaps the most important data to share are between the public and private sector.

Much progress could be made more rapidly if the public sector (e.g. academia) could share data with the private sector (e.g. Big Pharma), and vice-versa in the pre-competitive space.

Such cooperation could be a vital cog of making rapid progress towards improving prospects for a cure for some cancers. It cannot be legislated for, but would provide a major stimulus to progress.

Too many in academia take a snooty view of the private sector, frequently until they require financing for specific research. This approach needs to change and progress towards sharing information and data is a major challenge for this Moonshot and will require significant negotiation.

Biden makes a great point about *paywalls* surrounding published research.

The current journal model is difficult to justify.

A group of scientists find funding, complete their research and send the results to a Journal for publication. Following peer-review, the manuscript may be accepted for publication.

Too frequently, the authors are obliged to pay hundreds (or in the low thousands) for the privilege of their work being published in a journal and frequently have to transfer copyright of their original work to the publisher as a condition of publication.

Not only that, but anyone wanting an electronic copy of the research report is frequently obliged to pay several tens of dollars to have a copy.

Alternatively, they or their institution should pay thousands of dollars for journal subscriptions. This is a strange business model, which requires change: frequently the best medical research is published in journals which report millions of dollars of advertising annually.

All research should be published for free and it should be freely available to anyone who needs a copy to examine in detail. The current model is broke and needs fixing.

It's also difficult to argue with the recommendation to involve patients earlier in clinical trial design and focus. Clinical trial recruitment is a huge problem in the U.S.

Patients either don't know about the trials, or they're not consulted about how the trials are designed and targeted. Only 4 percent of all the patients with cancer in the U.S. are involved with a trial.

There is something to learn from the United Kingdom where many times that percentage are participating in clinical trials.

Apart from formulating specific areas requiring modification to improve the research situation, this Moonshot should also open the door for a re-think of a wide variety of potential impediments to making progress.

For example, within the Moonshot, it would be timely to re-evaluate the clinical trial paradigm of phase I, phase II and phase III.

Modern medicine has made some remarkable strides forward, particularly in the past decade, and it would appear timely to re-evaluate this paradigm so as to shorten the time it takes to do trials required for approval of a new drug without losing any important information about efficacy and safety.

In addition, much more consideration should be given to *effectiveness* as well as *efficacy*: trials are performed currently on highly selected groups of patients who are eligible to enter a trial because of strong restrictions laid down by entry criteria. Healthcare costs are a significant issue today, and there could be a profitable discussion about basing reimbursement and pricing on *effectiveness* rather than *efficacy*.

Value sits at the heart of this. The door is slightly open: let's take the opportunity to push it.

One pitfall to avoid is the Moonshot attempting to fix with injections of finance important issues that are not really related to a scarcity of money, but more to do issues such as vanity, commercial or academic conflict of interest, legal hurdles, poorly designed research (*reductionism*), and poor peer review (compounded by the enormous increase in the number of journals being published).

Failure to address such malfunctions of the scientific machinery could interfere with reaching the goals of the Moonshot.

Vice President Biden continued: "It's personal. But I know we can do this."

There is so much to be admired about the scope and organization of the White House Moonshot Initiative.

Apart from the specific goals, which will be

defined before the end of 2016, it provides a unique opportunity to allow broader and strategic thinking to take place around current barriers to progress, such as clinical trial design and FDA requirements for efficacy and safety before approval for general use not only of medicines but of other treatments such as devices where power morcellation has been a focus of many articles recently.

The final goals established are currently being discussed. The idea to measure progress by improving patient outcomes rather than counting publications is essential to its success. The focus of all cancer research should ultimately be to do something for the patient with cancer or someone who is at high-risk of developing the disease. It was timely to see the recent letter in The Cancer Letter from deans of schools of public health emphasizing the importance of *prevention*.

I have always struggled as to why there has not been such an effort to improve cancer outcomes on such a scale internationally: cancer is a global problem. Let's hope that the Moonshot is a success and that it can be a model to be taken up by top-level groups internationally.

Global society should not have to depend on the United States alone to solve one of the great problems of our times: the European Union at least should volunteer to share the financial burden (not to dilute federal government contributions by cost-sharing, but to add additional matching funds).

In such a way, more rapid progress should expected.

From a personal perspective, the Moonshot should have its main focus on the patient with cancer, but should not ignore other elements of cancer control.

Initial reports highlighted the search for a *cure*, but there are four pillars of Oncology: **Prevent** those cancers that can be prevented; **Treat** those cancers that can be treated; **Cure** those cancers that can be cured: and, provide **Palliation** whenever required.

The continually aging demographic worldwide will result in a continually increasing number of new cases of cancer being diagnosed every year. The U.S. will not be spared these increases, and the changing healthcare system, coupled with progress in drug delivery, will have many consequences including seeing more and more patients receiving chemotherapy being treated as hospital out-patients.

I have a special plea. I have experienced the deaths of my mother, father and younger sister from this vile disease.

Please Vice President Biden, pay more attention to the protection of care givers and the environment. Care giving is emotionally draining as well as having financial considerations. It can also be hazardous.

Certain types of chemotherapy excrete identified human carcinogens in the hours and days following treatment (e.g. adriamycin), in sweat, faeces, urine or vomit exposing care-givers to these dangerous chemicals.

In hospital, there are special procedures for dealing with such hazardous waste but these do not exist in the home environment.

General advice such as "restrict use of one toilet to the cancer patient" or "flush twice" do not solve the problem.

Apart from posing a threat to care givers and family members, these hazardous chemicals enter into our sewage systems and general environment and have been doing so on a daily basis for several decades.

I enthusiastically endorse the appointment of Vice President Biden to head up this important initiative. He has seen cancer at close up and has experience of what it is like to be a parent of a cancer victim and he has seen the situation of care givers at first hand. This group has been largely ignored until now.

The federal government, the cancer research community, the entire medical profession, the insurance industry, the pharmaceutical companies and politicians must join forces to fight this cause of human suffering on all fronts. America has taken the initiative: the rest of the world must follow their example and join in.

Godspeed, Mr. Biden.

The author is president of International Prevention Research Institute and University of Strathclyde Institute of Public Health at iPRI in Lyon ouest Ecully, France.

Capitol Hill

Senate Committee Looks to Fund Medical Innovation Legislation

By Conor Hale

Over 150 organizations sent an open letter to the leaders of the Senate Health, Labor, Educations and Pensions Committee, supporting them for advancing legislation that will form the basis of the Senate's version of the 21st Century Cures Act, which passed the House last year.

The Senate committee has passed 19 bills since February—collectively referred to as medical innovations legislation—which include agreements on NIH funding, support for the Precision Medicine Initiative, and changes to FDA and NIH hiring power. Now, the committee has to work to find ways to pay for the programs before sending the bills to the full Senate.

Committee Chairman Lamar Alexander (R-Tenn.) said his goal is to present the legislation to the Senate leadership combined with an NIH Innovation Fund that would provide a surge of one-time funding for priorities such as the vice president's National Cancer Moonshot Initiative Young Investigator Corps, the Big Biothink Awards and the BRAIN Initiative.

"With its 21st Century Cures Act passed last year, the House voted 344 to 77 to provide $8.8 billion in paid-for mandatory funding to support such NIH priorities," Alexander said April 6, after the committee approved the final five bills of the medical innovations package with bipartisan support. "We continue to work to find an amount that the House will agree to, the Senate will pass and the president will sign."

"The legislation would create a breakthrough path for new medical devices like the breakthrough drug path approved in 2012 that has already attracted 384 applications and led to 39 approvals," he said.

"It would give the FDA new authority to attract talented researchers, and reduce the administrative burden on NIH and researchers. It would target rare diseases, including diseases resistant to antibiotics. It would allow NIH to require researchers who use NIH funds to share their data. It would encourage interoperability of electronic medical records, reduction in excessive physician paperwork, clarify each patient's right to own their own medical record, and discourage information blocking."

The next day, during an appropriations subcommittee hearing on the FY2017 budget for NIH, Sen. Patty Murray (D-Wash.) said: "I was very pleased that in the recent budget deal, Democrats and Republicans were able to come together to boost discretionary investments in the NIH. That was an important step forward—but I don't see any reason to stop there." Murray is the ranking member on the HELP committee.

"That's why I've made clear, in my discussions with Chairman Alexander about legislation to advance medical innovation in the HELP Committee, that if we really want to get patients safer, more effective treatments and cures, we have to take advantage of every funding opportunity, including mandatory investments in the NIH. It's a make or break priority."

On April 6, the Senate HELP committee passed:

• **The FDA and NIH Workforce Authorities Modernization Act** (S. 2700), which increases the FDA's ability to hire and retain employees and pay them a salary more competitive with the private sector, and enables the FDA to more fully participate in the Biomedical Research Service to attract scientists.

• **The Promise for Antibiotics and Therapeutics for Health Act** (S. 185), which helps streamline approval of treatments for antibiotic-resistant bacteria.

• **The Advancing Precision Medicine Act of 2016** (S. 2713), supporting the president's Precision Medicine Initiative and efforts to map one million genomes.

• **The Advancing NIH Strategic Planning and Representation in Medical Research Act** (S. 2745), which requires NIH to develop a strategic plan every six years, and helps ensure the inclusion of women and minorities in research.

• **The Promoting Biomedical Research and Public Health for Patients Act** (S. 2742), which requires the NIH to cut inconsistent or duplicative reporting requirements for researchers, and also allows those performing clinical research supported by the National Center for Advancing Translational Sciences to conduct later-stage clinical trials.

"The Innovations effort encompasses a surge in funding for the National Institutes of Health," the 150 organizations wrote in their open letter to the HELP committee and Senate leadership April 27.

"The groundbreaking research NIH fosters, coupled with private sector investment and innovation, fuels our economy, grows jobs and most importantly saves lives. By putting more muscle behind NIH at a time of unprecedented opportunity for breakthrough progress, the Innovations initiative can—and will—shift the fight against deadly and debilitating diseases into high gear."

Led by Research!America, other organizations signing the letter include the American Heart

Association, the American Lung Association, and the Association of American Cancer Institutes, as well as several universities, health systems, cancer research centers, and professional societies. The full letter and list of organizations is available here.

PCORI Approves $44.4 Million for 21 Research Studies

The Patient-Centered Outcomes Research Institute approved $44.4 million in funding for 21 new patient-centered comparative clinical effectiveness research studies.

Several studies will focus on cancer, including comparing ways to improve colorectal cancer screening, develop a more patient-centered approach to assessing the quality of care for people with cancer, and assessing the effectiveness of different treatment strategies for ductal carcinoma in situ among older women.

The funds will also support projects focusing on a range of conditions and problems that impose high burdens on patients, caregivers, and the healthcare system, including post-partum depression, misuse of antibiotics, post-traumatic stress disorder among veterans, and joint replacement among others.

The board also approved several studies that aim to reduce disparities in care, including a project testing the effectiveness of several strategies for improving outcomes for children with Down Syndrome who do not have access to specialty clinics.

The cancer-related studies include:

• **Comparative Effectiveness Analyses Among Conservative Treatment Strategies for Ductal Carcinoma in Situ,** at Yale University, is a two-year project with a budget of $439,730. The principal investigator is Shiyi Wang.

The goals of this study are to compare benefits, treatment burdens, and side effects between less-intensive treatment strategies among older DCIS patients.

Among women older than 67 years with DCIS, the study plans to compare the outcomes of "biopsy only plus observation/active surveillance" versus "immediate BCS without radiation therapy," in terms of breast cancer-specific mortality, invasive breast cancer diagnosis, subsequent mastectomy, receipt of RT, and treatment burdens (including follow-up biopsy, imaging tests, and outpatient clinic visits).

Among older women with DCIS who have received BCS without radiation therapy, the study will compare the outcomes of receiving sentinel lymph node biopsy versus not receiving it, in terms of breast cancer-specific mortality, invasive breast cancer diagnosis, subsequent mastectomy, receipt of RT, and side effects (including lymphedema, pain, and limitation of movement of upper extremity).

• **Ostomy Telehealth for Cancer Survivors,** at the University of Arizona, is a three-year project with a budget of $2,080,650. The principal investigator is Robert Krouse.

A proposed ostomy self-management telehealth program, led by ostomy nurses with ostomy "peer-buddies" and patient/caregiver education and support, will use telehealth delivery to improve patients' ability to participate, especially for elderly, rural, inner-city, or poor-health cancer survivors with ostomies. The study will compare patients participating in the telehealth program with patients receiving usual care, according to PCORI.

The first goal of the study is to determine if the program improves patient ostomy self-management knowledge and skills and health-related quality of life, and if this improvement continues six months after completing the program. The second goal is to determine the differences in patients' use of family resources, use of medical care, and ostomy-related family financial burden between the program participants and patients receiving usual care.

• **Comparing Interventions to Increase Colorectal Cancer Screening in Low-Income and Minority Patients,** at Indiana University, is a four-and-a-half-year project with a budget of $2,880,644. The principal investigator is Susan Rawl.

The study will evaluate two interventions—a tailored DVD, and the DVD plus a patient navigator; compared with each other and with usual care—to increase CRC screening rates among a diverse sample of patients.

The study plans to enroll an ethnically diverse group of 750 men and women ages 50-75 who were referred and scheduled for colonoscopy at one endoscopy department but canceled or did not attend their scheduled appointment.

• In a previous set of approvals, in March, PCORI approved **Comparison of Operative versus Medical Endocrine Therapy for Low Risk DCIS: The COMET Trial,** a study being performed by the Alliance for Clinical Trials in Oncology. The five-year project has a budget of $13,399,702. The principal investigator is Shelley Hwang.

The primary objective of the study is to assess whether the invasive cancer rate in the affected breast is the same for women undergoing standard care compared to surveillance. Secondary objectives will be to compare mastectomy rate, survival endpoints, and quality-of-life endpoints between standard care and surveillance groups.

The large randomized trial will compare operative to medical endocrine therapy for low-risk DCIS. The study plans to compare patients with low-risk DCIS who are randomized to receive either standard care or surveillance. Patients randomized to the standard care group will choose between currently recommended treatment options including surgery and radiation; those in the surveillance group will be monitored closely, with surgery or radiation only upon progression of disease. Patients in both the GCC and AS groups will be free to decide whether to choose endocrine therapy. Study participants will be recruited at 100 participating study sites during the 48-month recruitment period, with 446 patients to each study arm.

PCORI's Board of Governors has approved more than $1.3 billion since 2012 in funding for 504 patient-centered comparative effectiveness studies and other projects to enhance the methods and infrastructure to support them.

Details of the approved projects can be found on PCORI's website.

In Brief

Pietenpol Named Vanderbilt Vice President for Research

JENNIFER PIETENPOL was named executive vice president for research at **Vanderbilt University Medical Center**, effective May 1.

Pietenpol will continue to serve as director of the Vanderbilt-Ingram Cancer Center. She is also the B.F. Byrd Jr. Professor of Oncology and a professor of biochemistry, cancer biology and otolaryngology.

According to Vanderbilt, Pietenpol will assume a portion of the responsibilities held by **Lawrence Marnett**, associate vice chancellor for research and senior associate dean for biomedical sciences. Marnett was named dean of basic sciences in the School of Medicine for Vanderbilt University.

In this role, Marnett will oversee the basic science departments, centers and institutes that are remaining with the university after the legal separation of the university and the medical center.

As executive vice president for research, Pietenpol will support the basic science programs in clinical departments, centers and institutes that will be housed in new VUMC. She will be responsible for leading the infrastructure that will advance much of the medical center's basic research enterprise.

As director of VICC, Pietenpol has successfully renewed Vanderbilt-Ingram's NCI designation as a comprehensive cancer center twice with exceptional merit ratings.

She has served on the Institute of Medicine's National Cancer Policy Forum. In 2008, she was appointed by President George W. Bush to the National Cancer Advisory Board.

She was a member of the board of directors of the American Association for Cancer Research, and serves on numerous other cancer-related scientific advisory boards including the Blue Ribbon Panel to advise the vice president's National Cancer Moonshot Initiative.

In 2012, she was elected as a fellow of the American Association for the Advancement of Science. She has received numerous honors for her research, most recently the Medical Research Advancement Award from the T.J. Martell Foundation.

MARGARET FOTI was honored at the 41st Annual Congress of the **Oncology Nursing Society** with the Honorary Member Award. Foti is chief executive officer of the American Association for Cancer Research.

The Honorary Member Award is awarded by the ONS to thank and honor an individual who is not otherwise eligible for ONS membership for his or her contributions to oncology nursing, support of the ONS, and conduct consistent with the ONS mission and core values.

Foti's formal recognitions include honorary degrees in medicine and surgery from the University of Rome La Sapienza and the University of Catania in Sicily, and an honorary degree in medicine from the University CEU of San Pablo in Madrid. Most recently, she was honored by the Society of Surgical Oncology with the 2016 James Ewing Layperson's Award.

During Foti's tenure as CEO, the organization's membership has grown from about 3,000 to more than 35,000 in 104 countries around the world.

JOHN WESTON was named chief operating officer and executive vice president of the **Prostate Cancer Foundation.**

Most recently Weston served as public affairs

department chair and chief marketing officer for the Mayo Clinic. He began his career at Mars Inc., held senior leadership positions at FedEx and was the chief marketing and corporate development officer for a valuation firm in Los Angeles.

Weston served on Mayo Clinic's Board of Governors and was executive director of the clinic's Office of Brand Management. He also served on the board of the Paralysis Project of America and was on the advisory boards of the Marriott School of Management, Brigham Young University and the University of Arkansas Walton School of Business.

AL BENSON III was elected president of the **National Patient Advocate Foundation's** executive board.

Benson is associate director for cooperative groups at the Robert H. Lurie Comprehensive Cancer Center of Northwestern University. He has served on the foundation's board for three years and also served on the scientific advisory committee since 2009.

"I am honored to serve as the National Patient Advocate Foundation's Board President. NPAF is a leader in fighting for improvements in the healthcare system at the state and federal level," Benson said. "We will continue our 20 year history of helping those living with serious illness by promoting bills like the Medical Debt Relief Act, 21st Century Cures, Innovation for Healthier Americans and other initiatives designed to address access and affordability issues for patients."

AVINASH DESAI was named vice president of Americas Oncology Medical Affairs for the Oncology Business Group of Eisai Inc., the U.S. pharmaceutical subsidiary of Eisai Co. Ltd.

Desai will lead Eisai's Oncology Medical Affairs team by creating and overseeing the medical strategy for the Oncology Commercial and Market Access businesses in the Americas. Desai, who has over 20 years of experience in the oncology field, will work closely with the company's clinical, commercial and OBG strategy organizations to develop, implement and deliver oncology life cycle plans. He will provide strategic leadership to the Medical Affairs team to ensure the delivery of key objectives.

Desai has designed and implemented clinical development and life cycle management plans for a variety of pharmaceutical products, including anti-angiogenic agents, taxanes, proteasome inhibitors, monoclonal antibodies, and targeted therapies. He has served as the global lead of Clinical Development and Medical Affairs teams, and has experience in strategic planning for product development, long-range project and life cycle management strategies, and the development of contingency plans.

Desai joins Eisai from Janssen Pharmaceuticals, Inc., where he was Global Medical Affairs Leader, Oncology responsible for leading the life cycle management of the company's oncology/hematology products. Prior to Janssen, he was director of International Clinical Development Oncology at Sanofi-Aventis, where he was responsible for the international development of oncology products in solid tumors and hematological malignancies and leading the NDA submission activities for several products. Desai also led the oncology clinical research/medical affairs department at Genaera Corporation.

MD ANDERSON CANCER CENTER named eight young researchers Andrew Sabin Family Fellows at an event honoring their benefactor, Andrew Sabin, and representatives of the **Andrew Sabin Family Foundation**. Eight cancer research fellowships providing $100,000 over two years are to be awarded annually in four categories: basic science, clinical, physician-scientist and population and quantitative science.

The inaugural recipients are:

Ken Chen, assistant professor of Bioinformatics and Computational Biology: Chen is involved in analyzing The Cancer Genome Atlas and the 1000 Genomes project data and has helped develop novel methods for precise characterization of heterogeneous cancer genomes and precision oncology.

David Hui, assistant professor of Palliative, Rehabilitation and Integrative Medicine and General Oncology: Hui focuses on cancer-related dyspnea and is involved in clinical trials examining interventions such as rapid onset opioids, corticosteroids and oxygen delivery modalities.

Nicholas Navin, assistant professor of Genetics and Bioinformatics: Navin aims to use single cell sequencing technologies to investigate tumor evolution in breast cancer patients and understand how they evolve resistance to chemotherapy.

Katharina Schlacher, assistant professor of Cancer Biology: Schlacher studies DNA replication fork protection at in-depth molecular and biological levels to provide biological insights and the framework to develop disease understanding, enabling prevention and treatment strategies.

Ferdinandos Skoulidis, assistant professor

of Thoracic/Head and Neck Medical Oncology: Skoulidis' research is building on his discovery of co-mutation-defined subsets of KRAS-mutant lung cancer, with a focus on identifying predictive biomarkers of response or resistance to immune checkpoint inhibitors.

Benjamin Smith, associate professor of Radiation Oncology and Health Services Research: Smith's research includes population-based survey studies of a statewide cohort of older breast cancer survivors and population-based research using registry and claims data.

Cullen Taniguchi, assistant professor of Radiation Oncology: Taniguchi studies hypoxia to find therapies that protect normal tissue from chemotherapy and radiation damage without compromising tumor kill.

Shannon Westin, assistant professor of Gynecologic Oncology and Reproductive Medicine: Westin's research focuses on the use of novel agents to treat gynecologic malignancies and the use of biomarkers to predict response and resistance to these therapies. She is the director of phase I trials in the Gynecologic Center.

Sabin has served on the MD Anderson Cancer Center Board of Visitors since 2005 and is president of Sabin Metal Corporation, the largest privately owned precious metals refiner and recycler in the country.

NATIONAL COMPREHENSIVE CANCER NETWORK published patient education materials for diffuse large b-cell, follicular, mantle cell, and peripheral t-cell lymphomas.

The NCCN Guidelines for Patients and NCCN Quick Guide series for Non-Hodgkin's lymphomas are available free of charge, and are sponsored by the Leukemia & Lymphoma Society.

NCCN Guidelines for Patients, translations of the NCCN Clinical Practice Guidelines in Oncology, are designed to provide people with cancer and their caregivers with state-of-the-art treatment information in easy-to-understand language, featuring patient-friendly elements, such as medical illustrations of anatomy, tests, and treatments.

KIDS V CANCER launched the Compassionate Use Navigator for the pediatric oncology community that provides up-to-date information on the compassionate use application process.

The Compassionate Use Navigator provides: an option for physicians to request help from Compassionate Use Navigator staff in completing a compassionate use application; step-by-step instructions on how to apply for compassionate use, including forms and templates; assistance in identifying points of contact at drug companies; and information on FDA and IRB rules for obtaining compassionate use medications.

In addition, the navigator aims to fill knowledge gaps about compassionate use by collecting data on the numbers and outcomes of applications. This data will lay the groundwork for developing next steps to improve access to drugs for those in dire need.

ALBERT EINSTEIN COLLEGE OF MEDICINE entered into a research agreement with **Jiangsu Hengrui Medicine Co. Ltd.** to develop innovative cancer therapies. The collaboration is the first between Einstein and a pharmaceutical company based in China.

Jiangsu Hengrui Medicine, established in 1970, is a fully integrated pharmaceutical company with annual net sales of over $1.2 billion. Hengrui's products and research span therapeutic areas including oncology and hematology, anesthesiology and pain management, cardiovascular and metabolic diseases, contrast media and inflammation.

THE WISTAR INSTITUTE and **Cormorant Pharmaceuticals AB**, a Swedish biopharmaceutical company specializing in cancer drug development, formed a partnership involving Cormorant's novel drug HuMax-IL8, which is undergoing a phase I trial at NCI.

"Wistar's biomarker analysis of the tumor samples will be instrumental in determining the effects of HuMax-IL8 on tumor immunosuppression," said Maarten de Château, CEO of Cormorant.

The lab of Dmitry Gabrilovich, the Christopher M. Davis Professor and program leader in Wistar's Tumor Immunology Program, has focused research efforts on abnormalities in the function of various myeloid suppressor cells. Gabrilovich and his colleagues have developed and validated a biomarker that will show if a tumor is inhibiting the immune system's response to the tumor by targeting the migration of myeloid cells to tumor tissues.

"This partnership provides us with the opportunity to assess the clinical utility of our new detection method of myeloid-derived suppressor cells in tumors," said Gabrilovich. "The evaluation of these cells directly in tumors is critically important for understanding the effect of the novel therapy developed by Cormorant."

MD ANDERSON CANCER CENTER and

Summit Medical Group in New Jersey announced the launch of their partnership to create the Summit Medical Group MD Anderson Cancer Center.

An extension of MD Anderson Cancer Center at Cooper in Camden, N.J., Summit Medical Group will now be clinically and operationally integrated with MD Anderson Cancer Center in Houston.

MD Anderson Cancer Center at Cooper joined MD Anderson Cancer Network, a program of MD Anderson Cancer Center, in 2013.

With a special emphasis on continuity of care, the new center will provide integrated, multidisciplinary cancer care for patients in northern New Jersey. The program, which provides medical oncology, infusion and diagnostic imaging, is already in place at Summit Medical Group's campus in Berkeley Heights.

Plans are underway to build a state-of-the-art, 130,000-square-foot building adjacent to Summit Medical Group's new facility in Florham Park, with future services to include radiation oncology. Groundbreaking is expected at the new site this summer.

GEISINGER HEALTH SYSTEM announced that 100,000 recruits have signed up for the health system's major biobank and DNA sequencing study known as **the MyCode Community Health Initiative**.

Launched in January 2014 in collaboration with the Regeneron Genetics Center, the MyCode Community Health Initiative originally set out to recruit 100,000 study participants. That target, however, was reached in only two years. Geisinger researchers have set a new goal of at least 250,000 participants.

Geisinger's study is also the largest in the United States that combines electronic health records linked to large-scale DNA sequencing data, according to the company.

ABBVIE will acquire **Stemcentrx** and its lead late-stage asset rovalpituzumab tesirine (Rova-T) currently in registrational trials for small cell lung cancer. The transaction is expected to close in second-quarter of this year.

Rova-T is a novel biomarker-specific therapy that is derived from cancer stem cells and targets delta-like protein 3 that is expressed in more than 80 percent of SCLC patient tumors and is not present in healthy tissue. Registrational trials for third-line small cell lung cancer are expected to complete enrollment by the end of 2016.

Rova-T is under investigation as a third-line treatment in SCLC, where there is no currently approved therapy. Rova-T has also been submitted to FDA for Breakthrough Therapy designation. Additional data on Rova-T, including overall survival data, will be presented at the 2016 ASCO Annual Meeting in June.

AbbVie will acquire Stemcentrx for approximately $5.8 billion in cash and stock. AbbVie will pay approximately $2.0 billion of the transaction value in cash and fund the remaining portion with stock. In addition, Stemcentrx investors are eligible to receive up to $4 billion in cash for additional, success-based milestone payments for the achievement of certain regulatory and clinical developments.

ABBVIE and **argenx**, a clinical-stage biopharmaceutical company, will collaborate to develop and commercialize ARGX-115, Argenx's preclinical-stage human antibody program targeting the immuno-oncology target GARP, a protein believed to contribute to immuno-suppressive effects of T-cells.

"ARGX-115 has been developed in collaboration with an outstanding team of academics at the de Duve Institute / Université Catholique de Louvain through our Innovative Access Program, which gives argenx rights to novel, exciting targets in our areas of therapeutic focus. We believe ARGX-115 has the potential to advance immuno-oncology by selectively targeting tumor immune escape pathways," said Tim van Hauwermeiren, chief executive officer of argenx.

"We are proud to develop and commercialize ARGX-115 through collaboration with AbbVie, a global leader in oncology. In addition to the attractive financial elements of this transaction, our shared interest in the commercial potential of ARGX-115, including the right to co-promote the drug in Europe, makes this a highly strategic collaboration for argenx."

Under the terms of the agreement, argenx will conduct research and development through IND-enabling studies. Upon successful completion of these studies, AbbVie may exercise an exclusive option to license the ARGX-115 program and assume responsibility for further clinical development and commercialization. Argenx will receive an upfront payment of $40 million from AbbVie for the exclusive option to license ARGX-115 and near-term preclinical milestones of $20 million. Argenx is also eligible to receive additional development, regulatory and commercial payments up to $625 million upon achievement of pre-determined milestones as well as tiered, up to double-digit royalties on net sales upon

commercialization.

Argenx has the right to co-promote ARGX-115-based products in the European Union and Swiss Economic Area and combine the product with its own future immuno-oncology programs. Should AbbVie not exercise its option to license ARGX-115, argenx retains the right to pursue development of ARGX-115 alone.

THE INDIANA UNIVERSITY Melvin and Bren Simon Cancer Center raised nearly $1.2 million for cancer research at its fourth annual Chuckstrong Tailgate Gala.

Hosted by the Indianapolis Colts and head coach Chuck Pagano at the Indiana Farm Bureau Football Center, the gala raised the funds through corporate sponsorships, live and silent auctions, and the annual Chuckstrong Giving Challenge. The total includes $250,000 given by the Jim Irsay family, and $50,000 from the coach and his wife, Tina.

The record-setting amount also included $30,000 raised from 25 people who paid $1,200 each for the chance to catch a touchdown pass from quarterback Andrew Luck. In all, the Chuckstrong initiative has raised $3.7 million for cancer research at IU.

Top-level "touchdown" sponsors for the event were Anthem Blue Cross and Blue Shield, DairyChem, the Efroymson Family Fund, Huntington Bank, Lilly Oncology, Sol and Kay Raso, the Throgmartin family, the IU Simon Cancer Center, the IU School of Medicine, and Indiana Knitwear.

Drugs and Targets

FDA Approves Cabometyx In Renal Cell Carcinoma

FDA approved Cabometyx (cabozantinib) tablets for the treatment of patients with advanced renal cell carcinoma who have received prior anti-angiogenic therapy.

Cabometyx, which was granted Fast Track and Breakthrough Therapy designations by FDA, is the first therapy to demonstrate in a phase III trial for patients with advanced RCC, robust and clinically meaningful improvements in overall survival, progression-free survival and objective response rate, according to the drug's sponsor, Exelixis Inc.

"The efficacy profile demonstrated by Cabometyx in the METEOR trial, now complemented by the overall survival benefit, is highly compelling," said Toni Choueiri, clinical director at the Lank Center for Genitourinary Oncology at Dana-Farber Cancer Institute. "Cabometyx is distinct from other approved treatment options, as it targets multiple tyrosine kinases involved in the development of RCC, including MET, AXL and three VEGF receptors."

The approval of Cabometyx is based on results of the phase III METEOR trial, which met its primary endpoint of improving progression-free survival. Compared with everolimus, a standard of care therapy for second-line RCC, CABOMETYX was associated with a 42 percent reduction in the rate of disease progression or death. Median progression-free survival for cabozantinib was 7.4 months versus 3.8 months for everolimus (HR=0.58, 95% CI 0.45-0.74, P<0.0001). Cabometyx also significantly improved the objective response rate compared with everolimus. These data were presented at the European Cancer Congress in September 2015 and published in The New England Journal of Medicine.

FDA granted Orphan Drug Designation to VAL-083 in the treatment of ovarian cancer.

The investigational drug candidate, developed by DelMar Pharmaceuticals Inc., previously received an orphan designation for glioma and medulloblastoma in the United States and glioma in Europe.

In more than 40 phase I and II clinical studies sponsored by NCI, VAL-083 demonstrated clinical activity against a range of cancers including lung, brain, cervical, ovarian tumors and leukemia both as a single-agent and in combination with other treatments.

"We are pleased to receive the designation, which is timely in light of new data presented this week with supporting the potential for VAL-083 in the treatment of ovarian cancer," said Jeffrey Bacha, chairman and CEO of DelMar Pharmaceuticals. "This announcement is representative of the progress we've made in developing VAL-083 which we believe positions the therapy as a viable treatment option for ovarian cancer patients."

DelMar's collaborators from MD Anderson Cancer Center presented preclinical data at the annual meeting of the American Association for Cancer Research, demonstrating that VAL-083 appears to have a distinct mode of action from platinum-based chemotherapies widely used in the treatment of ovarian cancer. In these studies, VAL-083 demonstrated an ability to circumvent cisplatin-resistance in all ovarian cell lines tested.