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Cancer Centers Join to Accelerate Trials, Industry Collaborations, Drug Development

By Matthew Bin Han Ong

Six NCI-designated cancer centers have agreed to pool data from their electronic medical record systems and cancer registries to accelerate discovery of targets and the development of biomarkers.

Launched in May 2014, the Oncology Research Information Exchange Network, or ORIEN, was founded by Moffitt Cancer Center and The Ohio State Comprehensive Cancer Center (The Cancer Letter, May 30, 2014).

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Conversation with The Cancer Letter

Dalton: I Don't Know a Place like ORIEN

The Oncology Research Information Exchange Network, a partnership of academic cancer centers, has collected data from over 120,000 patients, and recently added four institutions.

"I don't know of another place that actually follows patients and has the patients donate all their clinical data throughout their lifetime, and tissue to be studied, and allows them the right of contacting the patient," said Bill Dalton, CEO of M2Gen, founding director of the Moffitt Cancer Center Personalized Medicine Institute, and one of the founders of ORIEN.

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In Brief

Davidson Chosen as AACR President-Elect; Kim Appointed Director of FDA's DOP1

NANCY DAVIDSON was named president-elect of the **American Association for Cancer Research**. She will officially take the position at the AACR's Annual Meeting, being held April 18-22 in Philadelphia, and will assume the presidency in April 2016.

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ORIEN Partnerships to Expedite Trial Matching, Industry Projects

(Continued from page 1)

Recently, ORIEN added four cancer centers: City of Hope, University of Virginia Cancer Center, University of Colorado Cancer Center, and the University of New Mexico Cancer Center (The Cancer Letter, Feb. 27).

The partnership is pursuing these fundamental goals:

• Obtain patient tissue data across multiple institutions to expedite clinical trial matching and provide support for clinical decisions,

• Create a federated database that member organizations are able to use for research,

• Charge pharmaceutical companies and other potential clients for access to the data, and

• Accelerate targeted discoveries and therapies for cancer patients.

The collaboration has so far accrued data from approximately 120,000 patients. The four new partners would add 50,000 patients each year.

ORIEN is built around a standard consenting and processing protocol called Total Cancer Care.

To join ORIEN, each new member pays $30,000 a year to train staff and implement Total Cancer Care—efforts that are overseen by M2Gen, the Moffitt biotechnology and informatics company that runs ORIEN.

"It is fairly unique to use one protocol amongst all centers," said Bill Dalton, CEO of M2Gen, founding director of Moffitt's Personalized Medicine Institute, and one of the founders of ORIEN. "I don't know of another place that actually follows patients and has the patients donate all their clinical data throughout their lifetime, donate their tissue to be studied, and allows the right of contacting the patient.

"I don't know of another effort identical to this."

Centers that join ORIEN also agree to the same standard operating procedures for identifying and extracting data elements, as well as how bio-specimens are obtained, processed and stored.

"I think the data is extremely high quality," Dalton said to The Cancer Letter. "Again, in part because of the normalization process of using the same protocol. Every member has agreed on exactly which data elements they are going to share. That's big."

A conversation with Dalton appears on p. 1.

The news of ORIEN's expansion comes soon after the American Society of Clinical Oncology announced its partnership with SAP, a German multinational software corporation, to develop CancerLinQ, a database of electronic health records (The Cancer Letter, Feb. 20).

"I don't categorize anything like ASCO as a competitor. I look at it as a complementary effort," Dalton said. "ASCO's effort is extremely important, but they're doing something quite different than what we're doing.

"ORIEN is agnostic to electronic medical records. As I understand it, the ASCO effort is primarily involved in measuring quality of care at the point of care."

ORIEN is an outgrowth of Moffitt's collaboration with Merck Pharmaceuticals. That collaboration lasted for five years, between 2006 and 2011. During that time, Moffitt created a network of 17 regional hospitals in 10 states, enrolling close to 100,000 patients on its protocol.

Instead of sharing de-identified data, the Moffitt protocol prospectively consents patients upfront to allow life-long follow-up, as well as granting the researchers the right to study tissue and associated clinical data in a way that advances cancer treatment and research. Patients also consented to being contacted should any important developments occur in the treatment of their disease.

Two years ago, Dalton, then-CEO of Moffitt, began conversations with Ohio State's Michael Caligiuri, director of the James-OSU Comprehensive Cancer Center and CEO of the James Cancer hospital.

"The growth of ORIEN coincides with President Obama's [Precision Medicine Initiative] announcement and the recognition that molecularly targeted medicine holds tremendous promise for all disease, particularly cancer," said Caligiuri Feb. 23, announcing ORIEN's new partners. "We believe ORIEN illustrates a collaborative pathway to operationalize personalized medicine to help discover cures for more patients."

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Precision medicine is the goal of cancer care, said Scott Ness, the Victor and Ruby Hansen Surface Endowed Professor in Cancer Genomics, associate director for shared resources, professor of internal medicine, and director of the Analytical and Translational Genomics Shared Resource at the University of New Mexico Cancer Center.

"The genome is so complicated. For example, when we do an exome sequence of 50,000 variants on each person, what we're trying to do is decipher what all these variants mean," Ness said to The Cancer Letter.

"What these databases allow us to do is to divide the population into smaller and smaller groups to find variants and mutations to help us essentially link these variants to specific phenotypes so that we know how to better treat people.

"We're trying to build an integrated database platform that allows us to bring different kinds of information together. For example, the medical record information and the clinical trial, and the kind of samples stored from each patient will be available for us to analyze.

"We also want imaging information, and, of course, we want genomic information, and we want to integrate all these different things in order to have better clinical translational research opportunities, and also to build better care opportunities in clinical trials for patients."

ORIEN is less of a database and more of a network of databases, Ness said.

"Each institution will have its own databases, and they'll be connected through ORIEN," Ness said. "This is one of the critical things about ORIEN. It's not 'big brother.'

"It's a way for different databases, each of which is secure and separate, to interact in a limited, controlled way to get the most advantage for the patients and for the researchers, without having to deposit all the data somewhere."

It is not publicly known how many more cancer centers are in the process of joining ORIEN.

"A number," Dalton said. "Well, more than one."

ORIEN Not a "Top-Down Initiative"

Cheryl Willman, director and CEO of the University of New Mexico Cancer Center, said ORIEN is so appealing because it's an academic collaboration designed by cancer centers for cancer centers.

"I think most of the informatics initiatives have been driven top-down by NCI, and I think that's good, but I also think we need to be at the table for those communications, and we need to compare resources we have at our own institutions and work together," said Willman, the Maurice & Marguerite Liberman Distinguished Chair in Cancer Research and professor of pathology at the University of New Mexico School of Medicine.

As a federated database, ORIEN's inherent advantage over a central data repository is its flexibility, and the members' ability to fully control data use.

"Coming from our communities in the Southwestern U.S., the issues of genetic privacy, discrimination, ownership of data, and true community participation in research is critically important," Willman said to The Cancer Letter. "Our populations and underserved communities are very sensitive about sending their tissues and data to some central national clearing house or database where they lose control.

"They want control and engagement, and they deserve that. Without that, any consortium or research partnership is a non-starter for our population here in New Mexico and I really respect that."

Willman and Dalton have worked closely—Dalton grew up in Albuquerque, N.M., and is an alumnus of UNM. He has served on the University of New Mexico Cancer Center's advisory board for the past 15 years of Willman's tenure as director.

"He's really been crucial in helping me build the UNM Cancer Center. And I'm on Mike Caligiuri's board at Ohio State, so the three of us are very close friends and colleagues," Willman said.

"ORIEN for us is a game changer. The University of New Mexico Cancer Center has many features that distinguish it among the nation's NCI Cancer Centers," Willman said. "While we serve a small population, just under two million, we are the nation's fifth largest state in landmass, so our population is very geographically dispersed and frequently lacks access to healthcare.

"Secondly, we are the nation's only minority-majority state and over 50 percent of the patients seen at our Center are Hispanic or American Indian and these populations are affected by very different types of cancers than non-Hispanic whites.

"Finally, our center's formal consortium partners are two large Department of Energy laboratories [Los Alamos National Laboratory and Sandia National Laboratories], and we have integrated their significant scientific strengths in bio and nanotechnology, imaging, novel radioisotopes and advanced computing and informatics into our center's research programs.

ORIEN is particularly interested in the UNM Cancer Center's integrated informatics platforms that

link statewide screening and tumor registries—a system that Willman says NCI reviewers consider a "model for the nation" for how an NCI center should build academic-community partnerships and community clinical trials networks.

"To serve our population, starting 12 years ago, we built a statewide cancer clinical trials network based here at the UNM Cancer Center that now involves all of New Mexico's community health systems, and all of its community oncologists. That's quite unusual among the nation's NCI Centers. We were thrilled to be funded under the new NCI National Clinical Trials Network NCORP [National Community Oncology Research Program] with a perfect merit score of 10.

"We have one of the nation's first statewide tumor registries, which was the founding member of NCI's SEER registry program, and we have several state population screening registries, so we have a statewide HPV screening registry, we're building a statewide hepatitis C screening registry, and those registries are actually linked to our tumor registry so we can look at how our impact on cancer screening actually affects cancer outcomes.

"Also, 48 percent of my patients are Hispanic, and 10 percent of my patients are Native American, and they are affected by very different cancers than non-Hispanic whites or 'Anglos,' as we call them.

"We have really high rates of liver cancer, kidney cancer, ovarian cancer, leukemia, and gallbladder cancer—the Native Americans have the highest rate of gallbladder cancer in the world. We have very unusual cancers affecting our multiethnic population that don't tend to be the common cancers that you see in whites."

ORIEN will give the UNM Cancer Center and the people of New Mexico access to new targeted drugs that are difficult to acquire alone.

"While we have large numbers of minority patients with unusual cancer patterns, our overall population is not huge, so to be able to build and join a larger network where all of our patients are undergoing detailed genomic characterization, and consenting to being followed through their lifetime in Total Cancer Care, and then joining these five other cancer centers to open system-wide trials to make sure I can get targeted drugs for our unique patients, is a huge benefit to our Center and the people of New Mexico," Willman said.

"The NCI clinical trials program, the National Clinical Trials Network, which we participate in, is terrific, but often does not have clinical trials or drugs that focus on the cancers that affect our underserved minority patients and thus may not meet the needs of our patients, and that's a challenge.

"So through the TCC/ORIEN partnership, we hope to be able to extend our science and improve access for our patients to novel therapies. For us, this really great and critically important."

In turn, the UNM Cancer Center brings diversity to ORIEN.

"One of the things I'm very thrilled about is we're bringing a large population of minority and underserved patients to the network, and having them really participate in and benefit from research is great," Willman said. "We've already done and published a lot of work showing that Hispanic and Native American children affected by leukemia have very different mutations than White, or Asian, or Black children.

"So one of the exciting pieces of work we've done at our center that we've just presented was this new type of leukemia—it's called Ph-like ALL—which turns out to have a hugely complex spectrum of mutations involving kinases, and there are FDA-approved drugs that we can target them to.

"We have discovered, in both colorectal and leukemia that our population has very novel mutations, so we bring that research to the consortium, and in turn, we hope to get the drugs that target those mutations back for our patients. So to us, it's a total win-win. We're really excited.

"Our first project here is to open the Total Cancer Care protocol, which we're in the process of doing, and we are beginning to integrate our leaders into regular interactions with the TCC/ORIEN leadership at our partner institutions."

Data Ownership and Shared Governance

ORIEN allows its members to retain ownership of their data, and lets them control how or what their patient data would be used.

A partnership with ORIEN is not exclusive, Dalton said.

"What we're trying to do is augment the capability of these centers," Dalton said. "Depending on the use of the data, if it's already occurring, for example, in the ORIEN setting, then we ask that they not duplicate that effort.

"Any data that a member generates, they can use for any purposes that they would have ordinarily used it for. The idea of ORIEN data in the aggregate is that use is determined by the alliance members themselves.

"They do not have to participate in all projects that come to ORIEN, which are mediated through M2Gen, at least for industry. M2Gen will mediate that and then

we will ask, how many members of ORIEN, and who wants to participate in a given project.

"They don't have to participate, and if they don't want to, then their data won't be used for that. I think it's important to recognize ORIEN as a self-governed alliance. Partners don't give up their data, what they agreed to is to share their data, and they will share their data with like-minded institutions that also will share their data.

"You give and you get. That's the way it works."

Access to a larger database and joint projects with other cancer centers and industry makes ORIEN invaluable, said Dan Theodorescu, Paul Bunn Professor and director of the University of Colorado Cancer Center.

"ORIEN offers a wonderful opportunity to leverage the significant institutional investment in precision cancer medicine that we have made and facilitates and empowers the work by our faculty members by allowing them to access data and samples on thousands rather than hundreds of patients," Theodorescu said to The Cancer Letter. "It makes faculty more productive, and offers larger datasets to really make actionable and impactful discoveries.

"A unique aspect of ORIEN is that it's an academic effort aimed at helping faculty at all these cancer centers to mine data collaboratively. You set up the infrastructure for allowing investigators to bring their own ideas in mining big data. I can look up patients at my own center but shortly I will be able to sit in front of the computer and see what's happening across ORIEN for that tumor type.

"I strongly believe that this is the way that the field should be going, creating these large networks of collaboration.

"By virtue of ORIEN's size and the number of patients, studies that once required a single investigator to put together their own patient cohorts and then make phone calls and engage collaborators for larger validation studies can now be greatly facilitated and accelerated and done more cost effectively.

"ORIEN has the clinical trial matching aspect, which is really fabulous benefit for patients and for our phase I program."

The University of Colorado brings expertise in precision cancer medicine to ORIEN, Theodorescu said.

"We are the developers of the COXEN principle, a new method of examining tumors and based on their gene expression profile match patients to the best drug," Theodorescu said. "That principle is now being tested in a large national trial on SWOG.

"I believe biomarker development in ORIEN will be stimulated by the needs of cancer clinical practice guidelines in use today and by virtue of its power help to improve these by integrating precision medicine approaches for patients."

Making Trials Feasible for New Therapies

The University of Virginia Cancer Center decided to join ORIEN because it addresses patient and research needs that are missing in many other genomics efforts in the U.S., said Thomas Loughran, professor of medicine and director of the University of Virginia Cancer Center, as well as the F. Palmer Weber-Smithfield Foods Professor of Oncology Research.

"After a thorough review by our team we thought that it really had a lot of benefit for cancer patients throughout the country, and eventually throughout the world," Loughran said to The Cancer Letter. "The advantage of ORIEN was not only doing state-of-the-art genomic analyses, but most importantly, linking analyses to patient outcomes.

"We were very intrigued by that model. We also liked the business model, whereby pharmaceutical companies would have access to consortium efforts to either validate new targets and/or develop new therapies. Certainly, this is very important for our patients, since with increasingly complex genetics involved behind cancer, each of the cancers are becoming much, much more complicated.

"The number of patients available for targeted therapy of a specific mutation is becoming very small. So it's difficult to do a clinical trial of newer targeted therapies unless you have access to a large denominator of patients, which is what the network provides. That's the main goal, really, is to achieve scale where these trials will be feasible."

The UVA Cancer Center has been recognized for groundbreaking work in basic science, Loughran said.

"In terms of what UVA brings to the table, we've been designated by NCI since 1986," Loughran said. "We have a Center for Public Health Genomics—led by Steven Rich—which has a really stellar group of bioinformatics faculty.

"When you're talking to groups and trying to negotiate joining, they're definitely looking for strengths that the new partner might bring. I think Dr. Dalton was very impressed with the outstanding breadth of UVA science, our bioinformatics capabilities, and the quality of our tissue banks led by Chris Moskaluk, who is the head of pathology here.

"He has a very adept staff involved in quality

control in making sure that samples are acquired in a timely fashion from surgery. The quality of that bank has been acknowledged by receipt of several supplements from NCI that are very competitive, and available only to NCI-designated centers."

Loughran, who joined UVA in 2013, was the program leader of hematologic malignancies at Moffitt from 1996 to 2003.

"I know Bill Dalton quite well," Loughran said. "I know Dr. Dalton is thinking of expanding it internationally. Dr. Dalton's vision is to take this beyond cancer. So UVA as well as Ohio State are big health systems, which I think, eventually, will bring strength to the further development of the model to not only focus on cancer, but all health."

Interfacing with Other Projects

Selecting the best big data collaborative project for City of Hope was a challenge, said Steven Rosen, director of the City of Hope Comprehensive Cancer Center, and provost and chief scientific officer for City of Hope.

"There are so many alternatives," Rosen said to The Cancer Letter. "That's why I felt a great deal of comfort when I knew that we were going to partner with two very established, successful institutions that were actually slightly ahead of us in driving these activities."

ORIEN is completely aligned with what City of Hope wants to accomplish, Rosen said.

"I was approached by Bill Dalton, who is a dear friend, and he told me about the mission and vision for ORIEN, and it resonated with us," Rosen said. "I felt that partnering with Moffitt and Ohio State—they subsequently added UVA, UNM, UCCC and City of Hope—would give us an opportunity to rapidly advance our program in precision medicine, and to do something that would have a significant impact.

"We contribute a very large patient base as well as a great deal of experiences in registry data. We, like other institutions, will be doing molecular analysis on a significant percentage of our patients, and so we'll contribute to the overall infrastructure of ORIEN."

City of Hope has a strong portfolio in both the genotype and phenotype components of ORIEN, said Joyce Niland, the Edward and Estelle Alexander Chair in Information Sciences, associate director of cancer informatics, and professor of information sciences at City of Hope.

"We were moving in the precision medicine direction anyway, as are all the other institutions, so to join forces will allow us to make progress even more rapidly," Niland said to The Cancer Letter. "We have quite a bit of experience to bring on the phenotypic side of gathering data.

"For example, I ran the NCCN Data Outcomes Research Data Coordinating Center for 15 years, and a lot of those same principles and methods will apply to this project."

City of Hope, as well as University of Colorado Cancer Center, Moffitt and Ohio State are members of the National Comprehensive Cancer Network.

NCCN, an umbrella group that develops practice guidelines and pathways in oncology and publishes a compendium on the use of cancer therapies, is vying to expand its role as big data reshapes the field.

For-profit players include drug supplier McKesson, which has an alliance with NCCN to create clinical pathways and to produce software that will allow physicians to assess treatment options consistent with evidence-based standards.

The pathways and supporting software will also allow providers to consult coverage policies mandated by payers (The Cancer Letter, Nov. 30, 2012).

City of Hope is also part of CI4CC—Cancer Informatics for Cancer Centers—a nonprofit organization that provides a forum for academic research informatics scientists.

"I'm a founding member and on the board of directors. Warren Kibbe, who's at the NCI, and Sorena Nadaf at UCSF were the driving forces behind establishing this new collaborative group," Niland said.

CI4CC meets a few times each year and has many participating informatics groups from cancer centers around the country.

"It's a great forum for exchange of ideas and processes, ways to share data and systems, etc.," Niland said. "I'll be presenting on the ORIEN phenotypic disease registry at the next meeting, March 30-April 1 in Washington, D.C."

According to Niland, ORIEN and other precision medicine initiatives will need to develop common data definitions across all member institutions, regardless of software systems.

"We need to strive for more codified data captured at the point of care for secondary use in research, since the experts who are caring for the patients are the ones who have the real knowledge of the data about them, yet we don't capture this discrete data very readily in our EMRs today," Niland said.

"What we've been missing all these years is all the significant clinical, patient care, and outcomes data, so that we can merge those data with the tissue and

genomic information.

"I'm really looking forward to working with the other centers to build this common phenotypic database that we can share to speed the discovery process."

ORIEN will collaborate and interface with other Big Data groups in the future, Dalton said.

"I don't know who with, or what the question will be, but the intent is ultimately: we have something of value to contribute," Dalton said. "Have we addressed all the needs? No.

"So if we can work with someone else who is like-minded and maybe took a similar approach in terms of creating data systems, who is addressing another issue or need, then it would make a lot of sense for those institutions to come together.

"That's our philosophical position."

Conversation with The Cancer Letter

Dalton: ORIEN Will Redefine Precision Medicine in Oncology

(Continued from page 1)

Dalton spoke with Matthew Ong, a reporter with The Cancer Letter.

ORIEN was founded by Moffitt and The Ohio State Comprehensive Cancer Center. The new members are: City of Hope, University of Virginia Cancer Center, University of Colorado Cancer Center, and the University of New Mexico Cancer Center.

Matthew Ong*: How was ORIEN created?*

William Dalton*:* ORIEN was created because we realized that the nearly 100,000 patients enrolled in the Total Cancer Care protocol launched at Moffitt in 2003 and opened as a protocol in 2006, wasn't large enough for precision, biomarker-based cancer trials. In addition to increasing the volume of the patients we could study, we also wanted to partner with other cancer centers, because of the skillsets that they would bring to the effort.

So ORIEN was created to form a partnership amongst cancer centers who are like-minded, who want to create personalized medicine, or augment what they've already done in personalized medicine.

The motive for members that join ORIEN is to partner with patients, and through that IRB-approved protocol, create a genuine partnership, and share data. Sharing data, of course, then leads to sharing ideas, and sharing ideas leads to projects, and better discoveries.

The essence of ORIEN is to share and collaborate and learn.

MO: *Is it ready to be used?*

BD: Oh yes. It's being used. It's for real. Moffitt, obviously, has been using it. All members of ORIEN agree to use the same protocol and partnership. The protocol, at the time we partnered with Ohio State and formed ORIEN in 2014, had about 100,000 patients.

The James-OSU adopted the same protocol and very quickly, in a little less than a year, enrolled 8,000 patients. They are a magnificent partner, and also brought skillsets to the overall effort. We have been learning from them about things such as certain ways to approach patients in a meaningful way about enrolling in Total Cancer Care.

The data is there, the process is there, and we are doing projects together. When Ohio State and Moffitt formed the partnership in the beginning of May 2014, the idea was to work together, but also to work with industry—industry being primarily pharmaceutical companies that bring a wealth of resources, especially new drugs, but also the ability to do sponsored clinical trials. So they are a very important part of what we do in ORIEN.

Again, ORIEN's about big data, so it's about sharing, and using the same protocol. That's important, because the more harmonized you are in your approach to gathering data with the same standard operating procedures, then, the richer your data, and the more you are able to draw conclusions by sharing data.

What ORIEN has done, in terms of priority, is match patients who are in need of clinical trials, however, Total Cancer Care is a very holistic approach. A priority for ORIEN is to meet patient needs, and the patients who are at highest risk and in most need, if you will, are those who have relapsed following standard therapy, or those that we predict aren't going to do well with standard therapy.

So we're looking for new therapies that are target-based, and those agents could come from the cancer centers themselves, which we obviously support, but also the pharmaceutical industry. It's about partnerships, it's about collaborations. We are also in the process of doing molecular profiling on these populations so that we can ultimately predict what therapies these patients may benefit from.

We're learning from all patients in discovery, but we're also giving back to patients, and this is why they want to contribute. Patients want to contribute for two basic reasons: one, most patients are very altruistic—they want to give back, they want to improve the knowledge base and have others benefit. But the second is, they want other people following their health

by looking at their data in anticipation that they may need therapy, especially a clinical trial. So those are the things that we're focusing on.

MO: *How much does ORIEN cost per year, and what are the sources of funding for ORIEN right now?*

WD: ORIEN is not a company. ORIEN is an alliance based on a contractual agreement to use the same protocol, share data in a limited way, but that allows for sharing of data in a deeper way for specific research projects that could lead to publications.

It's funded at $30,000 a year per partner, which really covers basic infrastructure costs. M2Gen is the "service engine" behind ORIEN. It's the coordinating center amongst the centers and their projects, but it's also the storefront for industry, primarily pharmaceutical companies, to engage ORIEN members.

These projects with industry reduce the cost of participating in ORIEN, and covers some of the cost for enrolling patients in Total Cancer Care. Through M2Gen, pharmaceutical partners will underwrite some of this cost that it takes to consent the patient, process the tumor, do the molecular analysis, do the data management, and support the process.

MO: *And that came out of Moffitt's partnership with Merck?*

WD: That's right, the Moffitt-Merck partnership in 2006 was an excellent partnership. There was a period of exclusivity in working with other industry partners for five years, but this ended in 2012. This exclusivity, however, did not limit our ability to use data for clinical trial matching patients to best treatments. We still work with Merck, but we now have the ability to work with other pharmaceutical companies as well.

MO: *What do future partner universities, and current ones, have to pay to be a member of ORIEN?*

WD: It's a rather modest fee of $30,000 a year.

MO: *Is that a standard fee for everyone, or is it contingent on patient population and therefore the size of the data offering, say, a center has a million, and another has half a million?*

WD: No, no. It's what is necessary to cover the cost of us assisting the members in implementing Total Cancer Care in their institution, and education, training, and then overhead of meetings and things like that.

MO: *ORIEN has six member organizations now, right?*

WD: Yes, six members now.

MO: *How many partners does ORIEN seek, and is there an ideal end number?*

WD: If there is, I don't know. We'd like to be all-inclusive, to be frank. Part of the motive, also, for Total Cancer Care, was to partner with the community as well. It's often difficult for patients to go to a tertiary center like Moffitt, or Ohio State, the James.

Ultimately, what we'd like is to give every patient access to this knowledge base that we've created. Creating this data warehouse with information on patient outcomes over time, linked to generated molecular data, creates evidence of what's going to work for given populations.

We would like to see every patient have access to that. So in expanding ORIEN we consider whether it improves access for patients to this capability. That's a huge motivating factor.

Another factor in expanding ORIEN members is that the volume and the variety of the data that would be created.

So we seek ORIEN members who are serving populations who are underserved. For example, University of New Mexico sees more Native Americans than probably any other center in the United States, and, as an underserved population, you can imagine that that's a population we want to include.

We want to learn from them. They may have changes that are associated with their cancers that may provide a greater understanding of why these cancers occur, and vice versa. The more diverse the population, the more the population benefits, the more the science benefits.

So, accessibility, and diversity of the population studied are very important.

MO: *Speaking of access, who has access to ORIEN? Whom is it primarily intended for, and will ORIEN's data be open to the public, for instance, non-partners, pharmaceutical companies, and other researchers, or do they have to become partners?*

WD: Pharmaceutical companies don't have open access, unless they contribute to the database, and even when they do use the data, it is de-identified and done in partnership with an ORIEN member.

What every company agrees to is allowing generated molecular data to be used to help the patient find the proper clinical trial. This is true no matter who generates the molecular data. So, for example, Merck's

data at some point could actually be used to match patients to another company's trial, and vice versa.

We're working with, a significant number of pharma clients now—between 11 and 12, and they all agree that generated molecular data can be used to match patients to another clinical trial, that's the way it should be. So the whole effort is a very patient-centric effort, and what we're out to do is to create evidence of the value of therapies and different tests that matter.

ORIEN generates evidence of that value, and that then helps the patient, because you're more likely to get the best treatment at the right time.

MO: *So you're saying that pharma is the primary consumer for ORIEN?*

WD: Right now.

MO: *Do you think other agencies, such as FDA and NCI, would be using ORIEN?*

WD: We're all NCI-designated centers. NCI members have the right to use their data on an NCI project. We want to contribute to the overall NCI mission as well, and this is just one way we think we can do it.

MO: *Are the fees for pharmaceutical companies flat across the board, or does it depend on what they're looking for?*

WD: It depends on what they're looking for, and what we have to do to get it.

MO: *What is the nature of ORIEN's relationship with its partner members? Can universities be a part of ORIEN as well as other groups who are building databases? Is it exclusive?*

WD: No, it's not exclusive. What we're trying to do is augment the capability of these centers. Depending on the use of the data, if it's already occurring, for example, in the ORIEN setting, then we ask that they not duplicate that effort. Use ORIEN.

But it is non-exclusive. Any data that a member generates, they can use for any purposes that they would have ordinarily used it for. The idea of ORIEN data in the aggregate, is that use is determined by the alliance members themselves.

ORIEN is a self-governed alliance. All new members have a seat at the table, literally. We formed a steering committee for ORIEN. It is that committee that determines the use of the data in the aggregate, but each member owns their own data. This is a federated system, you're not just putting everything into one database that can be used for anything.

Members have a say about how their data is used. They do not have to participate in all projects that come to ORIEN, which are mediated through M2Gen, at least for industry. M2Gen will mediate that and then we will ask, how many members of ORIEN, and who wants to participate in a given project.

They don't have to participate, and if they don't want to, then their data won't be used for that. I think it's important to recognize ORIEN as a self-governed alliance. Partners don't give up their data, what they agreed to is to share their data, and they will share their data with like-minded institutions that also will share their data.

You give and you get. That's the way it works.

MO: *Are there any potential competitors? What is unique about ORIEN, and how does ORIEN stack up in terms of numbers and product offerings to potential competitors in oncology bioinformatics, such as ASCO's CancerLinQ and Google's Flatiron, for instance?*

WD: I think those are all important efforts. ASCO's effort is extremely important, but they're doing something quite different than what we're doing. As I understand it, the ASCO effort is primarily involved in measuring quality of care at the point of care. Very important.

But they're asking different things, and they're not doing research per se, so in that, they don't need a protocol to consent the patient.

What ORIEN is doing is chiefly research. We're asking patients to donate their data and tumors so we can study them. We can find new targets for new drug development, for example. We can find and develop new biomarkers that will predict response or non-response to therapy. We can use this information to enroll patients in clinical trials.

That's chiefly research, so I don't know if I would categorize these as competitors. I certainly wouldn't for ASCO. If anything, what we're doing is complementary, and I think that's what the overall effort of improving prevention and care of cancer is by, ultimately, a convergence of effort, if you will, and then, maybe, what you may see in the long run is as we individually develop our capabilities, you will see a network of networks.

I think everybody wants to see both the individual and society do better. Things like comparative effectiveness research, we can do that, because we're following patients throughout their lifetimes. We can do what's called a cohort analysis, and say, "Alright, for patients that look like this person, here are 10,000 patients that look like this person."

What we'd be able to do is to describe the person at the point of contact, and find the patients that are

most similar to this person being seen. Then you can ask, "What were the therapies used for that population that look most like this patient?" You then itemize the different therapies and ask, "What were the outcomes? What was the cost?"

That's comparative effectiveness. That's value to society. I think one way to look at any of these efforts is by value. Value to the patient, value to the physician who is trying to take care of this patient and to the researcher or advance the cause, and value to society.

What's the cost? I think, overall, maybe it's better to say, what's the value? We all want the best outcome, but at what cost from a societal point of view?

Again, I don't categorize anything like ASCO as a competitor. I look at it as a complementary effort. What they're doing is extremely important, I think what we're doing is extremely important, and as society evolves, we'll probably see a convergence of contribution.

MO: *Do you know if anyone is doing anything similar to ORIEN?*

DW: I don't, actually. It is fairly unique to use one protocol amongst all centers. I don't know of another place that actually follows patients and has the patients donate all their clinical data throughout their lifetime, and tissue to be studied, and allows them the right of contacting the patient.

I don't know of another effort identical to this.

MO: *Does ORIEN's range also include electronic health or medical records?*

DW: ORIEN is agnostic to electronic medical records.

What ORIEN does is use data from EMRs and cancer registries that are in a de-identified state, and that's the data that's shared amongst all members.

It's a dataset that has a limited number of elements, but it's enough for any member to do feasibility analyses. In other words, if they had a project in mind, but they needed more patients to study or more tissues to study, they can come to ORIEN and say, "How many patients in our system have this disease with this kind of tissue to be studied, and maybe already developed molecular testing?"

We can tell, and they can actually see for themselves.

That's the feasibility analysis. And if there are enough patients that could contribute to that project for that center, then that member would then go to the ORIEN steering committee and say, "I want to do this project, how many other centers want to join us?"

You're not mandated to participate in that project, but those that are interested deposit all their data into this data-mart that will support the project.

With ORIEN, everybody agrees to share some data on every patient that they've enrolled in Total Cancer Care at their institution. So you're getting an immediate survey of the landscape. If your analysis says this is feasible, then we invite others to now put their data together so everybody's studying it under the same conditions, which is exceedingly important.

MO: *Is that data quantifiable by the number of patients?*

WD: Right now we have approximately 120,000 consented patients in the Total Cancer Care warehouse, and approximately 38,000 clinically annotated specimens in the biorepository, and over 16,000 patients with associated molecular data.

Any person's particular specimen may be studied by multiple different institutions using different molecular assays. For example, all patient specimens who have had targeted exome sequencing performed also have gene expression analysis. By combining results of different assays we may gain insights about the systems biology of tumors and how this influences the clinical phenotype

MO: *So the focus here is patient tissue data. Does ORIEN include anything else, for instance, practice management and billing data?*

WD: Not yet. I can't tell you there won't be, and it may be that, depending on what the question is, and where the alliance members want to go. But right now, our focus is to generate data to discover mechanisms of tumor progression and then translating those discoveries into target-based clinical trials, and then matching the patients to the best clinical trials available based on the phenotype and genotype of that patient.

MO: *Is ORIEN financially self-sustaining right now?*

WD: Right now, it is.

MO: *Could you explain the mechanics behind Total Cancer Care, and why the protocol is crucial to ensuring the quality of data in ORIEN?*

WD: A common denominator for all members who join ORIEN is the agreement to utilize a common protocol, Total Cancer Care protocol. The protocol is fairly straightforward. The goal of the protocol is to identify patient need, and the needs of patients depend on where the patients are in their journey of dealing with cancer. That's why we ask patients if we may follow them throughout their lifetime.

The needs of a newly diagnosed patient are very different than the needs of a survivor. While there is

a heavy emphasis on understanding therapeutic need, we are also interested in psycho-social needs. We have patient self-reported instruments that are part of the Total Cancer Care effort. Patients complete the questionnaire at time of enrollment, and because patients have consented to be re-contacted, we may revisit the patient to determine if there are changes in habits or quality of life.

A major goal of the Total Cancer Care protocol is to identify patient need, and because we are studying large populations of patients, develop evidence-based approaches to meet need. The protocol also allowed us to re-contact the patient should we find something that could benefit the patient, such as a clinical trial.

By using a standardized protocol and consent, we are able to harmonize the effort for collecting and sharing data. By using essentially the same protocol and consent across all ORIEN institutions, we can be more confident that we are asking the same things of the patients so we can share data.

We have also agreed to the same standard operating procedures for identifying and extracting data elements, as well as how bio-specimens are obtained, processed and stored. Also, to date, most of the molecular studies performed on patient tumor specimens use the same molecular platform making comparisons between patients more valid. So today, we believe using a standardized protocol upfront creates a more harmonious approach for following patients throughout their lifetime and allows for comparisons between patient populations.

MO: *Let's back up a little to M2Gen. When was it created?*

WD: M2Gen was created by Moffitt in 2006, because we needed a dedicated workforce to implement and operationalize the TCC protocol. We knew that while Moffitt saw a lot of new patients, the numbers were not enough to address the questions we were asking.

So we started partnerships with hospital communities throughout Florida and other states, all adopting the same protocol, same procedures. M2Gen was created to implement Total Cancer Care, not only at Moffitt, but at the community sites as well. And we used funding, partly from the pharmaceutical industry, but also from the state of Florida.

The state and the county provided about $30 million for this effort. This commitment from the Florida community allowed M2Gen to engage and operationalize the TCC protocol at community sites, which also provided greater access for patients who could not travel to Moffitt. We also believed that engaging the community at large would allow for comparative effectiveness research and a means of addressing the value of new treatment practices.

We started seeking strategic partners from the pharmaceutical industry, and eventually partnered with Merck, an ideal partner. They got the big picture.

Merck created a pre-competitive space, and recognized that molecular data generated for research should be available for patients who could benefit from a target-based clinical trial, no matter who sponsored the clinical trial.

Since then, every pharmaceutical company who has worked with M2Gen has recognized that data generated for research may be available to identify patients who should be tested for qualifying diagnostic tests associated with target-based clinical trials, no matter who sponsors the trial.

This principle is very important and serves as a means of enriching patient populations who can be screened for inclusion in clinical trials.

M2Gen is wholly owned by Moffitt, so it's a subsidiary of Moffitt dedicated totally to the Total Cancer Care effort. That, and M2Gen serves as a vehicle for the pharmaceutical industry to have access and develop private-public collaborations with Moffitt, and now other ORIEN members, for new drug discovery and clinical trials.

MO: *What is Moffitt's role, then, in ORIEN? Is it providing data, and who pays for what?*

WD: There is still some monetary support from Moffitt to M2Gen, but Moffitt also basically developed the protocol and the approach that others have adopted. Obviously, most of the data in the data warehouse originated at Moffitt, because Moffitt started enrolling patients in 2006.

But what we've agreed is, Moffitt will share this data with those that contribute to the data. If you contribute, you get access to it.

So Moffitt's a member, and participates in the governance of ORIEN, just as all the other members do. Moffitt's contribution was the protocol, all the data generated to date, and there is intellectual property that's been created in the process of developing Total Cancer Care that has also been licensed to ORIEN, but we're not asking any of the members to pay for that.

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This is Moffitt's contribution to ORIEN.

MO: *Who is responsible, say, within M2Gen, for the quality of the data?*

WD: Ultimately, me. But I fortunately have got a lot of smart people that work in this area. Our chief bioinformatics officer and chief scientific officer has a Ph.D. in bioinformatics and astrophysics. His name is Hongyue Dai.

He was the leader of bioinformatics at Merck prior to coming to M2Gen and was the primary architect in designing the molecular platforms to study specimens obtained from patients enrolled in the TCC protocol.

It has worked out beautifully. He's brilliant, and knows the data really well.

MO: *So M2Gen is also the one responsible for the technical IT infrastructure of the database.*

WD: M2Gen is a platform that operationalizes Total Cancer Care. We're chiefly an information company, and we're here to support other centers, but we're also here to coordinate partnerships between the members, and partnerships between industry and members. That's M2Gen's job.

MO: *How consistent and high quality is the data presently, and how do you expect hat to grow?*

WD: I think the data is extremely high quality. Again, in part because of the normalization process of using the same protocol. Every member has agreed on exactly which data elements they are going to share. That's big.

MO: *Would you say it's as complete as it can be right now?*

WD: Well, I think the "as can be" is key here. We have a favorite saying at Moffitt and M2Gen, and now, ORIEN: "If you're doing your job properly, your job's never done." Because we're constantly learning and we're constantly trying to improve how we do things. That is a constant, and there are still major challenges.

If you ask what's the ideal size, I don't know what the ideal size is. But we have to consider as we grow that we would need to be able to deliver to those members that are there, and M2Gen's only so big, so the growth will be paced.

We have to accomplish what we're there to accomplish. We have to be there for the members of ORIEN. If we take on so many that we can't accommodate, then we made a mistake.

So the long-winded answer to your question about how many more we can integrate depends on how many we can serve. Ideally, our principle is, improve accessibility, improve quality, and improve affordability.

MO: *We briefly talked about a "network of networks" in the future—how do you envision ORIEN's role will be in that context, and will ORIEN collaborate and interface with other groups?*

WD: For that I can say, yes. I don't know who with, or what the question will be, but the intent is ultimately: we have something of value to contribute. Have we addressed all the needs? No.

So if we can work with someone else who is like-minded and maybe took a similar approach in terms of creating data systems, who is addressing another issue or need, then it would make a lot of sense for those institutions to come together.

That's our philosophical position.

MO: *How are Moffitt and Ohio State engaging physicians, hospitals and patients right now in the development of ORIEN?*

WD: Moffitt and Ohio State finding each other was critical, because you had like-minded institutions who actually thought very similarly, liked each other, and knew it was going to happen, but it still took 2.5 years to figure out how that would happen.

And that was very important that we basically set up, if you will, the rules of engagement, which are now gaining input from the new members as they are coming in. You have to be flexible.

How we're engaging patients is, for example, at Moffitt and soon to be at Ohio State, we created an informative video. The first thing we did about 6 years ago was we created a patient advocacy and ethics counsel. We knew we were pushing the envelope on some of this.

So these were advocates and ethicist from across the nation as well as local, and we would ask them questions, one of which was, "What could we give back to every patient that participates? Not just those that might need us for clinical trials matching, but every patient?"

And without hesitation, the advocates said, "Give us back our own information in a way we can use it." That was the birth of the patient portal. At that time, it was strictly at Moffitt—it was one of the most popular things we've ever done.

Patients want to know what's happening to them, why, and they want to see the same information, and we've learned a lot about how to communicate with patients, how to engage them, and make them true partners with their physicians.

We've created tools, such as patient self-reporting, and that's structured, so we get family

history, social history, all kinds of important quality of life that the patient revisits periodically, and it's a means of communicating to us. The patient can look at their own consent form, if they have questions about their consent, then they're told who to contact and how about questions they may have.

As ORIEN is formed and has more members, we are creating a Total Cancer Care website that's just beginning, so that no matter where a patient is in the nation or in, maybe, the world, they can access their data, and learn what's being done, with their data, and they can review their consent, those kinds of things—similar to what we've done in Moffitt, but what we're going to do is put it on a national, and global scale. That's one of the major priorities.

MO: *What's the feedback like from patient advocacy organizations?*

WD: ORIEN is in the process of requesting advocates and ethicists to come together as an advisory board. What we have done previously was for Moffitt and Total Cancer Care, but it's much bigger now. We're just beginning the effort of recapitulating the group we had for Moffitt and now for ORIEN. It's an extremely important group, and we're looking forward to having that input—can't do it without them.

MO: *How have the conversations been with other universities and cancer centers? Has it been, "Oh, here's ORIEN, this looks really interesting. We want to join," or "We're ORIEN, we're great, please join us"?*

WD: Both. We've approached centers, but centers approached us, too, which is great. We started with Ohio State, which was very important because we knew we needed to co-develop this thing—but it's not, "Join Moffitt!" It's, "Let's form something."

That's what had to happen and with Moffitt and the James at Ohio State, they formed something. And now, as we're getting more members, they're bringing their skillsets and input, and almost immediately, we're getting different insight from the perspective of the various institutions, which is fabulous.

At some point, you've got to make decisions about where you're going to go, but you can see, of the members, just from geography alone, we've spanned the nation, and the populations that these centers serve are quite unique. That's all very valuable, and they're all extremely high profile, high quality institutions.

We're thrilled. All ORIEN members are very happy to be there, and happy that other members are there. We hope that continues to grow, but we have to recognize that we can't grow so fast we can't accommodate what we're there to do.

MO: *How many cancer center partners are in the works right now?*

WD: A number.

MO: *Just a number?*

WD: A number. Well, more than one. Again, paced growth; that's the best way to put it.

MO: *It's been a year since The Cancer Letter last heard from ORIEN, so what and when will the next big announcement be? What's the next step?*

WD: Total Cancer Care was put together to identify need and meet need. Right now, our major priority for us is, "Who has the greatest need?" and in our mind, it's patients who either stop responding or aren't responding to standard therapy and need new therapies and new clinical trials.

That's the effort that you're going to see ORIEN members focusing on. Again, we'll do that in collaboration with NCI—we're all NCI members. We like to think of ourselves as part of the solution. We don't claim to be the whole solution; we want to part of the solution; we want to contribute to the other efforts that are ongoing.

But I think you're going to see a lot of effort on target discovery, biomarker analysis and development that will predict response or non-response to patient populations, and then utilizing this information to match the patient to the best clinical trial that's most suitable for them.

And because patients are being followed throughout their lifetime, we think we're in a good position to anticipate need. So that is a major goal for us. It's one thing to identify need and then meet that need, but if you could anticipate that need—that's where we think we can come in because we're studying these large populations, and you'll start understanding, well, patients that look like this ultimately develop a specific need.

Rather than wait for the need to manifest, we will try and anticipate the needs of high-risk patients.

We think we can actually do that with clinical trials. That's our primary goal.

U.S. Prescription Drug Spending Increased 13 Percent in 2014

New hepatitis C therapies with high price tags and the exploitation of loopholes for compounded medications contributed to a 13.1 percent increase in U.S. drug spending in 2014, a rate not seen in more than a decade, according to the 2014 Express Scripts Drug Trend Report.

Hepatitis C and compounded medications are responsible for more than half of the increase in overall spending. Excluding those two therapy classes, 2014 drug trend (the year-over-year increase in per capita drug spending) was 6.4 percent.

Specialty medications—biologic and other high cost treatments for complex conditions, such as multiple sclerosis and cancer—accounted for more than 31 percent of total drug spending in 2014.

In related news, cancer drug prices have increased by 10 percent annually, an average of $8,500 per year, from 1995 to 2013, according to a study published by the National Bureau of Economic Research (The Cancer Letter, Jan. 23).

According to an Express Scripts forecast last year, specialty drug trend more than doubled in 2014, to 30.9 percent. Hepatitis C medications accounted for 45 percent of the total increase in specialty spend despite having the second lowest prescription volume among the top 10 specialty conditions.

Medicare plans—required to follow Medicare Part D formulary guidelines—were the hardest hit, as their annual specialty drug spend increased 45.9 percent.

"For the past several years, annual drug spending increases have been below the annual rate of overall healthcare inflation in the U.S., but that paradigm is shifting dramatically as prices for medications increase at an unprecedented and unsustainable rate," said Glen Stettin, senior vice president of clinical research and new solutions at Express Scripts.

"Now, more than ever, plans need to tightly manage the pharmacy benefit, implement smarter formularies, control compounded medication use and offer the right clinical support to ensure all patients are able to achieve the best possible health outcomes at a price our country can afford."

The U.S. spent nearly 743 percent more on hepatitis C meds in 2014 than it did in 2013. New treatments for hepatitis C are just one example of non-orphan drugs with orphan-drug price tags. Future pharmaceutical innovations, such as new cancer drugs and PCSK9 inhibitors for high blood cholesterol, will continue to challenge payers.

Projected to command an annual cost as high as $10,000 per patient, and potentially reaching a patient population eventually as large as 10 million Americans, PCSK9 inhibitors alone could one day cost the U.S. healthcare system an estimated $100 billion per year.

In Brief

Nancy Davidson Chosen as President-Elect of AACR; Kim Named Director of FDA's Division of Oncology Products 1

(Continued from page 1)

Davidson is director of the University of Pittsburgh Cancer Institute and UPMC CancerCenter.

Davidson is a breast cancer researcher whose work focuses on clinical and translational breast cancer research, cancer biology and treatment, and the role of apoptosis and mechanisms of epigenetic regulation of gene expression of the estrogen receptor alpha gene in breast cancer treatment.

"With deaths from cancer declining and the number of cancer survivors on the rise, this is an exciting time in cancer research and care. I am honored to be given the opportunity to work with AACR and its members on our singular focus to advance scientific discoveries that can translate to exceptional patient care," said Davidson, who is also distinguished professor of medicine and pharmacology and chemical biology, associate vice chancellor for cancer research, Hillman professor of oncology, and professor at the Clinical and Translational Science Institute at the University of Pittsburgh, and also adjunct professor of oncology, Johns Hopkins University School of Medicine in Baltimore.

"We are delighted that Dr. Davidson has been elected to serve as the next AACR president-elect," said Margaret Foti, chief executive officer of the AACR. "She is an acknowledged expert in breast cancer research whose clinical and translational work has had a profound impact on the lives of patients. Dr. Davidson will lead the association with much energy and dedication, and it will be an honor to work with her to make further strides in our mission to prevent and cure all cancers."

Prior to joining the University of Pittsburgh in 2009, Davidson was professor of oncology at Johns Hopkins University School of Medicine and director of the Breast Cancer Program at Johns Hopkins Oncology

Center. Early in her career, she was a research assistant professor of pharmacology at the Uniformed Services University of Health Sciences.

Davidson was elected by the membership as a member of the AACR board of directors from 2002 to 2005, and has been actively involved in the AACR since 1988. She is an editorial board member of Cancer Prevention Research and has served on numerous other boards and committees, the most recent of which are: member of the AACR Distinguished Lectureship in Breast Cancer Research Award Committee (2012); chair (2011) and member (2010) of the Nominating Committee; member of the AACR Outstanding Investigator Award for Breast Cancer Research Committee (2010); member of the Continuing Medical Education Committee (2009-2014); chair of the Breast Cancer Research Foundation-AACR Grants for Translational Breast Cancer Research Scientific Review Committee (2009); member of the Dorothy P. Landon-AACR Prize for Translational Cancer Research Committee (2009); chair (2008-2010) and member (2005) of the Research Grant Review Committee; member of the Stand Up To Cancer Innovative Research Grants Scientific Review Committee (2008-2009); member of the Scientific Program Committee for the AACR International Conference on Frontiers in Cancer Prevention Research (2008); and member of the AACR Award for Lifetime Achievement in Cancer Research Committee (2005).

Davidson is known for her studies involving the role of hormones and the estrogen receptor in breast carcinogenesis that have defined the molecular mechanisms driving the disease as well as for her efforts to establish novel therapeutic approaches for patients who fail to respond to common treatment modalities. She has led clinical trials involving chemotherapy and endocrine-related therapies for treating premenopausal breast cancer and has increased the understanding of the potential of angiogenesis inhibitors, such as bevacizumab for treating metastatic breast cancer.

She has received the AACR-Women in Cancer Research Charlotte Friend Memorial Lectureship, the Potamkin Award from the Pennsylvania Breast Cancer Coalition, the Gianni Bonadonna Breast Cancer Award from the American Society of Clinical Oncology, the Distinguished Alumna Award from Johns Hopkins University Alumni Association, and the Rosaline E. Franklin Award for Women in Science from the NCI.

She is also an elected member of the Institute of Medicine, the Association of American Physicians, and the American College of Physicians. Davidson is also a past president and former board member of ASCO and currently serves as a member of the scientific advisory committee of Breakthrough Breast Cancer and the scientific advisory board of the V Foundation for Cancer Research.

GEOFFREY KIM was named director of the Division of Oncology Products 1 in the **FDA Office of Hematology Oncology Products**.

Kim serves as the acting deputy director in DOP1. He is involved with numerous cross-center working groups, developing policies pertaining to in-vitro companion diagnostics, combination products, and dose finding optimization strategies for oncology products.

Kim is also the gynecologic malignancies scientific liaison for OHOP and is active with outreach to the ovarian cancer community through the Society for Gynecologic Oncologists, Gynecologic Oncology Group, and the Ovarian Cancer National Alliance.

Kim will report to Richard Pazdur, director of OHOP. His appointment becomes effective March 22.

"Geoff brings a great deal of both clinical and regulatory expertise to the position that will be required as oncology rapidly advances in the future years," Pazdur said.

Kim joined as a medical officer in DOP1 in 2010.

He received his bachelor's degree at UCLA, his medical degree at the New York Medical College, and completed his residency in internal medicine at the Montefiore Medical Center in the Bronx.

He performed laboratory research at these institutions with a particular focus on cell adhesion molecules and cellular signaling. Kim completed his medical oncology fellowship at NCI, where he was active in both laboratory and clinical research in the NCI molecular signaling section and the ovarian cancer clinic.

"I would like to thank Dr. Amna Ibrahim for serving as the acting division director of DOP1 during the transition period," Pazdur said in an email to the OHOP staff. "Dr. Ibrahim will assume her previous role as the deputy division director of DOP1."

The job was previously held by Robert Justice.

SAGAR LONIAL was named chief medical officer, and **CHARLES STALEY** was named chief quality officer of **Winship Cancer Institute of Emory University**. Both physicians joined Winship's senior leadership team.

Lonial is a professor and executive vice chair of Emory's Department of Hematology and Medical

Oncology. His research focuses on B cell malignancies, including multiple myeloma.

Staley, a professor and director of Emory's Division of Surgical Oncology, specializes in the management of patients with gastrointestinal cancers. He previously served as Winship's chief medical officer and now assumes responsibility for the institute's quality improvement processes across all disciplines and campuses.

KEVIN BEHRNS was named co-editor-in-chief of the journal **Surgery**, as well as a member of the executive committee of the board of governors of the American College of Surgeons. Behrns is chairman of the University of Florida College of Medicine's department of surgery and the Edward R. Woodward professor of surgery.

Behrns has served on the editorial board of Surgery for more than 10 years and succeeded former co-editor **Andrew Warshaw**, surgeon-in-chief emeritus at Massachusetts General Hospital and the W. Gerald Austen professor of surgery at Harvard Medical School. Behrns's co-editor is **Michael Sarr**, a professor of surgery at the Mayo Clinic.

Behrns said he wants to help the journal establish a dynamic social media presence, enhance its electronic edition and mobile accessibility, and find engaging new ways of communicating with young surgeons.

In his new role on the board of governors, Behrns will chair the college's membership services pillar. This group manages humanitarian medical efforts, such as the organization's response to the 2010 earthquake in Haiti. The group also oversees the college's international chapters.

INDERBIR GILL was appointed chair of global initiatives for the **American Urological Association**, effective June 1.

Gill serves as the founding executive director of the University of Southern California Institute of Urology and as chairman and professor in the department of urology and associate dean of clinical innovation at USC's Keck School of Medicine.

Gill will be responsible for the association's International Education Plan and will assist in identifying new global opportunities and collaborations with various national and multi-national urological societies. He will also serve as editor of the AUA's Global Connections publication.

He has been recognized with multiple awards from the medical, surgical and urological communities, including the Dr. B.C. Roy National Award, presented by the president of India; the St. Paul's Medal, presented by the British Association of Urologic Surgeons; and the USC Presidential Medallion, the highest annual academic honor bestowed by USC.

In addition to being a member of the AUA, Gill is a member of the American Association of Genitourinary Surgeons and the Clinical Society of Genitourinary Surgeons.

UNIVERSITY OF VIRGINIA Health System and **Novant Health** announced their intent to create a Northern Virginia regional health system. The proposed agreement would include UVA Culpeper Hospital and all of Novant Health's Virginia facilities, including Novant Health Haymarket Medical Center, Novant Health Prince William Medical Center and Novant Health Cancer Center. Final details are anticipated to be announced in July 2015.

Representatives from UVA and Novant Health have begun discussions to create a joint operating company for UVA Culpeper Hospital and Novant Health's Virginia operations by June 30. The discussions will include how Novant Health and UVA can integrate or coordinate cancer care across Northern Virginia. Under the proposed arrangement, UVA and Novant Health intend for each of the hospitals in the regional health system to continue directly employing all existing staff.

THE WORLD MOLECULAR IMAGING SOCIETY will collaborate with **NCI** to promote best practices for co-clinical trials.

Co-clinical trials are defined as parallel or sequential trials of combination therapy in patients and in mouse and human-in-mouse models of appropriate genotypes to represent the patients. The initiative is designed to help establish best practices for quantitative imaging methods and imaging protocols that are applied to both mouse and human-in-mouse models.

As part of the agreement, WMIS will include two spotlight sessions on precision medicine and co-clinical trials during the upcoming Annual World Molecular Imaging Congress September 2-5, in Honolulu, Hawaii. The theme of the meeting is Precision Medicine, Visualized.

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VARIAN MEDICAL SYSTEMS was selected to equip and service two new national proton therapy centers in England with the Varian ProBeam proton therapy system. Under a public tender, Varian was selected as the preferred supplier to provide equipment and service to operate two three-room centers to be constructed in London and Manchester in a contract valued at up to £80 million.

Varian expects to conclude and sign the contract and book the equipment portion of the order in the summer. Equipment installation is expected to take place beginning in August 2017, with patient treatments expected to begin from 2018. The UK's two national proton therapy centers will be located at University College London Hospitals NHS Foundation Trust and The Christie NHS Foundation Trust in Manchester.

A group of cancer researchers, in collaboration with **Apple Inc**. and **Sage Bionetworks**, launched a mobile app that breast cancer patients track their symptoms and progress.

The app, titled Share the Journey: Mind, Body and Wellness after Breast Cancer, is an interactive research study that aims to understand why some breast cancer survivors recover faster than others, why their symptoms vary over time and what can be done to improve symptoms.

It uses surveys and sensor data on the iPhone to collect and track fatigue, mood and cognitive changes, sleep disturbances and reductions in exercise.

"One reason to build these apps and run these studies is to see whether we can turn anecdotes into signals, and by generating signals find windows for intervention," said Stephen Friend, president of Sage Bionetworks and a principal investigator for Share the Journey. "We're most interested in disease variations and the hourly, daily or weekly ebb and flow of symptoms that are not being tracked and completely missed by biannual visits to the doctor."

Apple and Sage were advised in development of Share the Journey by Patricia Ganz at UCLA's Jonsson Comprehensive Cancer Center, Ann Partridge and Judy Garber at Dana-Farber Cancer Institute, Kathryn Schmitz at the University of Pennsylvania Perelman School of Medicine and Susan Love at UCLA and the Dr. Susan Love Research Foundation.

Share the Journey is one of five apps being launched in conjunction with Apple's ResearchKit. The developers also are creating a Spanish-language version of the app and planning to expand the study to other countries. The app is available for download from the iTunes App Store.

Drugs and Targets

FDA Approves Unituxin For High-Risk Neuroblastoma

FDA approved Unituxin (dinutuximab) as part of first-line therapy for pediatric patients with high-risk neuroblastoma.

Unituxin is an antibody that binds to the surface of neuroblastoma cells. Unituxin is being approved for use as part of a multimodality regimen, including surgery, chemotherapy and radiation therapy for patients who achieved at least a partial response to prior first-line multiagent, multimodality therapy.

The FDA granted Unituxin priority review and orphan product designation. With this approval, the FDA also issued a rare pediatric disease priority review voucher to United Therapeutics, which confers priority review to a subsequent drug application that would not otherwise qualify for priority review. This is the second rare pediatric disease priority review voucher granted by the FDA since inception of the rare pediatric disease review voucher program, which is designed to encourage development of new therapies for prevention and treatment of certain rare pediatric diseases.

The safety and efficacy of Unituxin were evaluated in a clinical trial of 226 pediatric participants with high-risk neuroblastoma whose tumors shrunk or disappeared after treatment with multiple-drug chemotherapy and surgery followed by additional intensive chemotherapy and who subsequently received bone marrow transplantation support and radiation therapy.

Participants were randomly assigned to receive either an oral retinoid drug, isotretinoin (RA), or Unituxin in combination with interleukin-2 and granulocyte-macrophage colony-stimulating factor, which are thought to enhance the activity of Unituxin by stimulating the immune system, and RA.

Three years after treatment assignment, 63 percent of participants receiving the Unituxin combination were alive and free of tumor growth or recurrence, compared to 46 percent of participants treated with RA alone. In an updated analysis of survival, 73 percent of participants who received the Unituxin combination were alive compared with 58 percent of those receiving RA alone.

Unituxin carries a Boxed Warning alerting patients and health care professionals that Unituxin irritates nerve cells, causing severe pain that requires treatment with intravenous narcotics and can also

cause nerve damage and life-threatening infusion reactions, including upper airway swelling, difficulty breathing, and low blood pressure, during or shortly following completion of the infusion. Unituxin may also cause other serious side effects including infections, eye problems, electrolyte abnormalities and bone marrow suppression.

Unituxin is marketed by United Therapeutics.

FDA granted Fast Track Designation for HS-410 (vesigenurtacel-L) for the treatment of non-muscle invasive bladder cancer.

HS-410, developed by Heat Biologics Inc., is a NMIBC product candidate based on the company's Immune Pan Antigen Cytotoxic Therapy platform, which is designed to generate killer T cells to attack cancers. HS-410 is currently being evaluated in a randomized phase II trial in combination with BCG and as monotherapy for the treatment of NMIBC.

FDA granted Orphan Drug Designation for Reolysin for the treatment of cancer of the fallopian tube.

The designation was granted on the basis of December 2014 application for an Orphan Drug Designation encompassing ovarian, fallopian tube and primary peritoneal cancers which are generally treated as one indication. On Feb. 11, Reolysin's sponsor, Oncolytics Biotech, announced that it had received Orphan Drug Designation for ovarian cancer.

"The FDA's recognition of ovarian and fallopian tube cancers as distinctly separate indications paves the way for a more targeted approach to the treatment of gynecological cancers," said Brad Thompson, president and CEO of Oncolytics. "We are pleased to have secured our third Orphan Drug Designation in the United States and look forward to continuing our development and commercialization program for Reolysin." Reolysin has also received a designation for pancreatic cancer.

Oncolytics has two sponsored clinical studies assessing Reolysin in the treatment of cancers of the fallopian tube. The first was a phase I/II clinical trial (OSU-07022) for patients with metastatic ovarian, peritoneal and fallopian tube cancers using concurrent intravenous and intraperitoneal administration of Reolysin that provided evidence of viral targeting and replication in peritoneal and ovarian cancer cells.

The second is an ongoing randomized phase II trial (GOG186H) of weekly paclitaxel versus weekly paclitaxel with Reolysin in patients with persistent or recurrent ovarian, fallopian tube or primary peritoneal cancer. The second trial completed enrollment in September 2014.

A new study found that capping the cost-sharing for prescription drugs on individual policies in the health insurance marketplace would reduce patients' annual out-of-pocket healthcare spending, and have a small effect on insurance premiums while allowing insurers to remain compliant with the law.

The study, commissioned by the Leukemia & Lymphoma Society and performed by Milliman Inc., examines the impact of imposing dollar limits on out-of-pocket costs for patients who purchase their insurance through health exchanges established under the Affordable Care Act.

The study measures how these dollar limits would reduce patients' out-of-pocket costs, the implication for insurers that must meet Actuarial Value Calculator requirements, and the impact on premiums for these plans. The study finds that the majority of benefit plan options examined can be accommodated with either no adjustments to other benefit features or with minor adjustments.

The study analyzed the effect of different levels of caps on prescription drugs: $100; $150; and $200 per 30-day supply, as well as an annual maximum set at 20 percent of the total out-of-pocket maximum. The study used examples of actual exchange plans found in the market to model the alternative designs.

The study finds that all four potential benefit design changes would reduce patient cost-sharing while the actuarial value would still comply with the requirements. The one exception would be in a modeled bronze level insurance plan, which would require further benefit design changes to keep the plan in compliance with actuarial values.

In addition, the study found that most of the caps modeled could be made with premium impacts under 0.5 percent in some cases with adjustments of $5 or less to other copayments. Again, the bronze plans remain the exception, where caps would need to be higher to keep premium increases nominal.

The full study is available on the LLS website.