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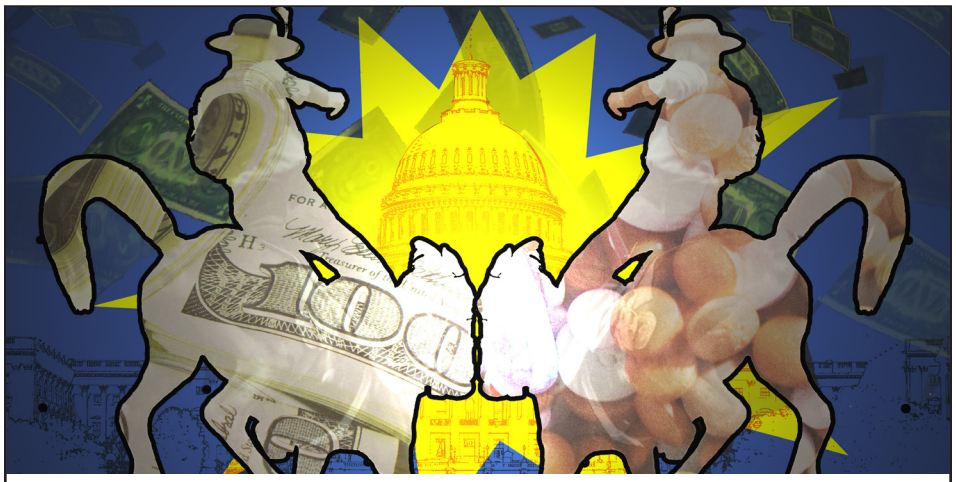

CMS Drug Payment Experiment Heads Toward Showdown on Capitol Hill

By Paul Goldberg

A demonstration project in which the Centers for Medicare& Medicaid Services hopes to investigate the impact of reimbursement based on Average Sales Prices of drugs is running into strong opposition, as a large number of cancer groups submitted public comments urging the agency to abandon the endeavor.

The agency's stated goal for tweaking the ASP-based reimbursement formula is to learn whether it gives physicians the incentive to prescribe the most expensive treatments available.

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Conversation with The Cancer Letter

Agus: $200 Million Interdisciplinary Institute to Focus on Data Modeling

A few years ago, at dinner with technology entrepreneur Larry Ellison, David Agus, director of the University of Southern California Center for Applied Molecular Medicine, mentioned his dream of opening an interdisciplinary cancer research center.

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Slamming the Door

Part XII: Scientists Vote with Their Feet

By Paul Goldberg

In their op-ed piece, Gilman and Sharp stated what it would take to fix CPRIT's problems. That was the polite version of the Gilman Plan.

The spoken version was more blunt: get rid of the "assholes" on the oversight board, jettison the administrators, then—maybe—CPRIT's credibility would be restored.

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Drug Payment Experiment Heads Toward Capitol Hill Showdown

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Opponents—including oncology professional groups and pharmaceutical companies—say that experimentation with ASP-based reimbursement, which is currently set at ASP plus 4.3 percent, will make it economically unfeasible for oncology practices to treat Medicare patients. (The Cancer Letter, March 11).

The demonstration project would be implemented in two phases:

• The first phase would involve changing the 6 percent add-on to the Average Sales Price—which is used to make drug payments under Part B—to 2.5 percent plus a flat fee, in a budget-neutral manner.

• The second phase would implement value-based purchasing tools similar to those employed by commercial health plans, pharmacy benefit managers, hospitals and other entities that manage health benefits and drug utilization.

Altogether, 1,261 individuals and organizations have submitted comments to the CMS docket, most of them protesting the demonstration project.

Sign-on letters and Congressional letters are being generated, bills are being drafted, and showdowns on Capitol Hill loom. The wrangling evokes memories of the 2007 effort by Congress to force CMS to abandon its National Coverage Decision to limit the use of erythropoiesis-stimulating agents (The Cancer Letter, July 20, 2007). That effort produced a sign-on letter from 224 House and 46 Senate members, as well as a bill to vacate the agency's action, but was unsuccessful.

"The assumptions and emphasis of the Part B Drug Payment model are misplaced," ASCO President Julie Vose wrote in a letter submitted to FDA as part of public comment.

"Providers do not control drug pricing, often lack bargaining power to negotiate lower acquisition prices, and providers should not be required to choose between providing care at a financial loss or sending patients outside of their practice for treatment.

"If the Administration's goal is to lower drug prices, this demonstration is not designed to achieve that outcome," Voss wrote. "Rather, the proposed demonstration places doctors and Medicare beneficiaries in the position of making impossible choices without directly addressing the underlying problem of high drug prices.

"If the goal is to bluntly cut payments for oncologists—and by CMS' own analysis, the proposed demonstration will achieve that goal—then this should be treated as a change in the statutory provision that sets that payment and not presented in the guise of a demonstration project."

Researchers from the Memorial Sloan Kettering Cancer Center's Center for Health Policy and Outcomes defended the underpinning of the CMS project. The ASP schema allows doctors and hospitals to earn more by administering higher-priced drugs and, more importantly, the ASP add-on allows drug companies to raise prices continuously, without impacting the prescribers.

A report by the group, led by health services researcher and former CMS official Peter Bach, says the system is self-perpetuating:

"There is a highly consistent pattern of price increases by an average of 1.7% every two quarters (3.3% per year) for the top 14 Part B drugs used by oncologists that have not been affected by entry of generic substitutes," the report states.

The report includes a graph that illustrates the price increases focusing on the reimbursement rates per unit and displaying the findings on a log scale, so that inflationary trends can be compared across different price ranges.

"Rising prices of Part B drugs over time are likely compressing the profit margins for medical oncologists from below," the report states. "One possible benefit of the lower profit percentage in the Medicare pilot might be that it will discourage pharmaceutical manufacturers from raising prices further, which would lead to savings for Medicare and beneficiaries (the flat fee add-on contributes little to this phenomenon for very high priced drugs). An alternative effect of the pilot is to place oncologists in a position where they are losing money

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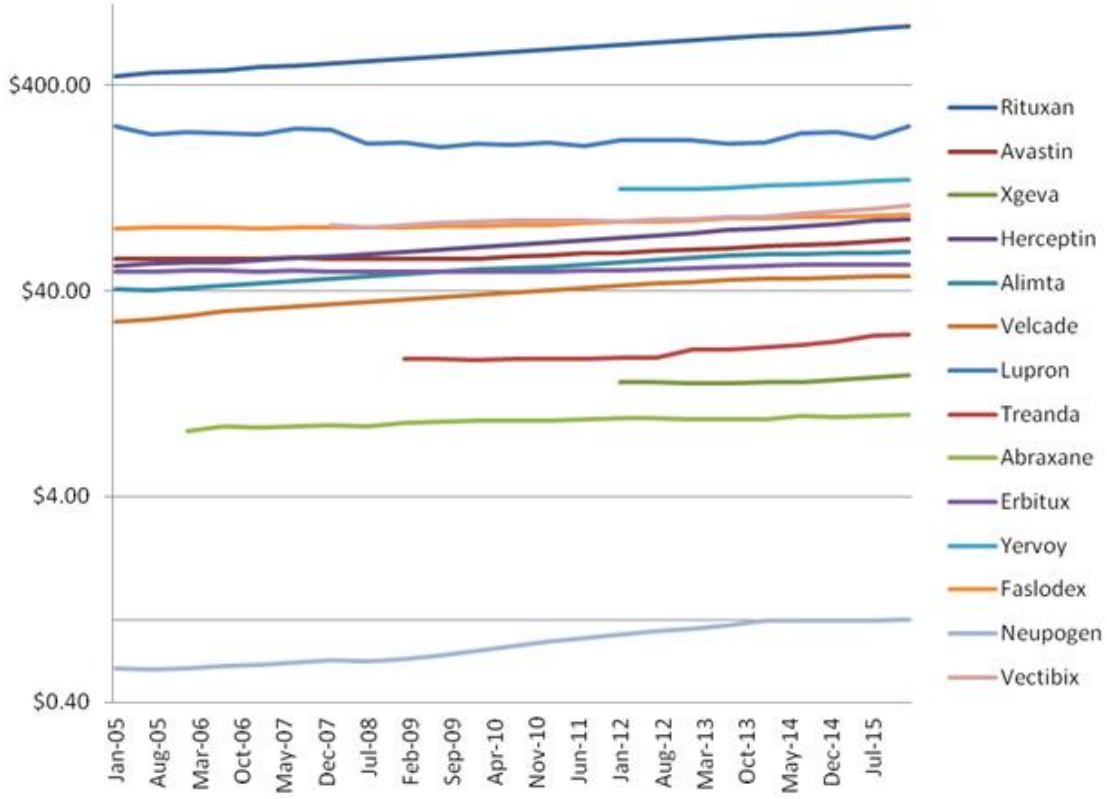

Inflation of ASPs of Part B drugs over six-month intervals. According to the report by Bach, et al., "rising prices of Part B drugs over time are likely compressing the profit margins for medical oncologists from below. One possible benefit of the lower profit percentage in the Medicare pilot might be that it will discourage pharmaceutical manufacturers from raising prices further, which would lead to savings for Medicare and beneficiaries (the flat fee add-on contributes little to this phenomenon for very high priced drugs). An alternative effect of the pilot is to place oncologists in a position where they are losing money on expensive drugs due to company's price inflation."

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ASP at any given time is calculated based on prices paid two quarters earlier, which means that the combination of add-ons over ASP and the price hikes in effect lock in price inflation, the report states.

"From these groups we are hearing very little about the pressure that price hikes are putting on their margins," Bach said to The Cancer Letter. "They seem to be either accepting the notion that price hikes companies institute to raise their revenues should be supported by taxpayers and cancer patients."

Bach's center recently received a $4.7 million grant from the Laura and John Arnold Foundation, a Houston-based philanthropist couple, to fund his research on drug pricing.

Health Subcommittee of Energy & Commerce Hearing Next Week

Meanwhile, a showdown is brewing on Capitol Hill.

On May 17, the Subcommittee on Health of the House Committee on Energy and Commerce will hold a hearing focused on the "patient and doctor perspective" on the CMS project.

The hearing is pegged to a bill, H.R. 5122, that would preclude CMS from going forward with the demonstration project.

On May 10, a group of 20 House members signed a letter in support of the demonstration project.

"Almost every day I hear from my constituents—including seniors and people with disabilities on Medicare—about the burden of high prescription drug costs," said Rep. Jan Schakowsky (D-Ill.), one of the authors of the letter.

"Those high costs mean many don't fill prescriptions or don't take full doses. That's why we support the Medicare proposed rule to test new value-based payment models for Part B prescription drugs. Those models will give us the data we need to make sure people get the most appropriate medications without having to pay too much."

On the Republican side, Rep. Renee Ellmers (R-N.C.) said the proposal would "affect an overwhelming number of patients receiving Part B drugs and severely limit their access to important and life-saving prescriptions, including chemotherapy treatments."

"Additionally, the proposed payment model fails to take into account the sequester cuts already in place," said Ellmers, author of a bill that seeks to exempt chemotherapy and other physician-administered drugs from being subject to cuts. "However, my legislation, H.R. 1416, does so by exempting chemotherapy and other physician-administered drugs from cuts based on average sales price.

While many cancer and pharmaceutical groups appear to oppose the CMS demonstration project, AARP and the American Academy of Family Physicians support it. "Last year Medicare Part B spent $22 billion on prescription drugs, double the amount spent in 2007," Nancy LeaMond, chief advocacy and engagement officer at AARP, said in a statement. "This spending escalation is simply unsustainable. We cannot continue to ask taxpayers and Medicare beneficiaries to pay for exorbitantly priced prescription drugs without any consideration of whether their money is being well-spent."

The CMS public comment docket includes letters from patients who seem convinced that they would lose access to care if the project, which is being introduced as a proposed rule, is implemented.

"I have four cancers," wrote William Johnson, a Missouri cancer patient. "My doctors tell me they will not keep me as a patient if this passes. Please look for new ways to cut costs from the insurance companies not the doctors."

The American Cancer Society Cancer Action Network similarly objects to the CMS experiment.

"ACS CAN is deeply concerned by the proposed Part B Drug Payment Model as it could negatively impact access to critical prescription drugs for cancer patients who need treatment and the providers who treat them," ACS CAN President Chris Hansen said in a statement.

"While the goal of the proposed demonstration project is to improve patient quality and lower spending, in its current design the model could actually result in cancer patients getting care in higher cost, less desirable settings," Hansen said. "We are exceedingly concerned that the scope and breadth of the proposal go far beyond a demonstration project and could result in beneficiaries having to travel greater distances in order to receive their cancer care. This result would be particularly problematic for beneficiaries who reside in rural areas who have fewer treatment options."

The letter from the society's public affairs arm is available on the ACS CAN website.

The Community Oncology Alliance argues that the CMS proposal is not a payment model.

"Colleagues at COA and I have been working with CMMI [the Centers for Medicare & Medicaid Innovation] for close to 3 years on the development of a real oncology payment model," said Bruce Gould, president of COA and medical director of Northwest Georgia Oncology Centers in Marietta, Ga. "And in the blink of an eye, without any stakeholder input, CMS comes up with a dangerous experiment on seniors – one we simply will not let them implement."

COA's comments are posted here.

On its website, COA attacks the MSKCC group and Bach, its top researcher.

"The quality of analysis and poor understanding of oncology care presented in this report by the MSK team is extremely disappointing," COA wrote in an unsigned critique.

"For instance, the report's lead author, Dr. Peter B. Bach, is not a medical oncologist but rather board certified in internal medicine, pulmonary medicine and critical care medicine. He does not provide chemotherapy treatment to cancer patients, and does not make the drug choices necessary to formulate treatment plans. The remaining co-authors are a hematology/oncology fellow with less than a year of clinical experience, an assistant research biostatistician, and data assistant."

Conversation with The Cancer Letter

Agus: $200 Million Institute To Focus on Data Modeling

(Continued from page 1)

"I said, it really would be an amazing thing if we could start to get people in one place and have residences, so the greatest physicists, mathematicians, engineers can actually come in and live there and be engrossed in cancer," said Agus, professor at the Keck School of Medicine of USC and the USC Viterbi School of Engineering.

"Well, how much would it be to kind of put together such a building and program?" Ellison, Oracle Corporation's chairman of the board and chief technology officer, said to Agus at the time.

"You know, about $200 million," Agus said.

"Done," Ellison responded.

The gift was announced May 11.

The Lawrence J. Ellison Institute for Transformative Medicine of USC will combine interdisciplinary research with holistic prevention and treatment of cancer. Agus will lead the institute.

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

Matthew Ong: *How did the Ellison Institute come about? Whose idea was it and how did it happen?*

David Agus: Who I blame for this, in the beginning, is a remarkable woman who used to be the deputy director of the National Cancer Institute, named Anna Barker. She came up with this program called Physical Sciences in Oncology, and the idea very simply was to kind of mix different disciplines—physical sciences with what we all do in the oncology world and put them together. It changed my research focus, it changed everything in how I think about the disease. It really has been transformative.

So my lab now is physicists, mathematicians, and engineers; it was going very well. And I would tell Larry Ellison about this—we would meet as friends, and we would have dinner and I would talk about this. He saw my excitement. Then I said, "It really would be an amazing thing if we could start to get thinkers in one place and have residences so the greatest physicists, mathematicians, engineers can actually come in and live there and be engrossed in cancer."

About four or five years ago, I got invited to the Aspen Ideas Festival with Murray Gell-Mann, the physicist who discovered the quark and string theory; he won the Nobel Prize in 1969, when I was four.

He interviewed me on cancer and how he questioned me opened my eyes to thinking about new things. He made me realize that physicists, engineers, and mathematicians view the world differently than we do. And almost by definition, we in the cancer world haven't succeeded, because we're still losing the war on cancer, so we need new ways of approaching it.

If we get to make the place where they can come and actually see, smell and be a part of the disease, we can really approach things differently.

And Larry said, "Well, how much would it be to kind of put together such a building and program?" I said, "You know, about $200 million." He said, "Done." And I said, "What?"

I almost fell off my chair. And he said, "To me, money doesn't mean anything, but progress does, and I really want to make a difference, because I've had some of my closest friends and relatives die of this disease."

His mother died at a young age, and he wanted to make an impact. This was perfect—it really aligned. I didn't ask him for anything, but he just jumped forward and said, "I get it, I want to be a part of it."

MO: *Will the Ellison Institute be the first of its kind in oncology?*

DA: I really think it's the first of its kind of a place that melds the sciences together in an experiential way to attack cancer.

Certainly, there are labs across the country that do that in physical sciences, but this is a dedicated institute with the residences—the hope is that it becomes not one institution—but with these residences, whether you're at Harvard or Oxford or the University of Copenhagen, you can come here and experience it. The war on cancer is not institution-by-institution; we're all fighting the same enemy.

We really want to put together a place where we can all work as a team and bring in people and whoever the experts are, wherever they are, to work as part of that team.

The center is planned to open in approximately two to three years. The center is operational today on a research basis, just without a formal residence.

MO: *Will the institute be part of USC Norris Comprehensive Cancer Center, or is it independent? Is it under any particular umbrella, school or department at USC?*

DA: The good thing is we're not under one department. It's a separate institute that reports to the provost, which I think is powerful, because in today's world, only one department gets credit for a grant or this and that.

We want to rise above that. Clinical care is part of the Norris Cancer Center, but we are a standalone institute that's part of USC, affiliated with Norris.

The NIH funds the conservative work remarkably, and I love that. But when you get gifts like this, you have to push the limits, try to do things differently.

MO: *How will the $200 million investment be used?*

DA: The building, which is about 110,000 square feet, will have a cancer clinic, and it will have a wellness clinic, because of the continuum there we need to study.

It will have an engineering lab for people to rotate in with an idea, and if the idea works, they stay, and if it doesn't, they go back to where they were at the university.

They'll have a think-tank, where people can talk and converse about these ideas. They'll have the residences. Also, the place will have a technology center, where there will be DNA sequencing, metabolomics, proteomics—they'll all be there.

The building's going to be designed so that students can walk around and tour and see these remarkable technologies and be engrossed and hopefully become aspirational for them to go into the field. It will be designed so they can go on these tours without disturbing the occupants in the labs or the clinics. Patients will have a choice as to whether they want to be in a place where people actually watch you getting your treatments to demystify it for people as a part of the education process, or it can be private. The patient will have that choice.

Our job, while we treat cancer, is to change how we treat cancer. So it really is meant more to study and learn than to be a high-volume clinic. Most of the money is going for the building, the technology to go inside the building, and there is a significant portion that is left to help run the program, and that, together with our NIH grants and other support from other foundations, is going to allow us to hopefully continue to run this and really make a difference.

MO: *I note that there will be emphasis on transformative and holistic medicine, and especially data. What are the specific research goals for the new center?*

DA: Our goal is very simple: to make a difference. But one of the things we realized early on, is that data is paramount. There will be a program where we're starting to gather data from around the world and be a repository for data—in a privacy-protected way—for researchers to analyze large datasets, potentially harmonize together and make them larger, and to really push the limits of Big Data as it applies to the field of cancer and progress.

To us, data is critical. At the same time, we're going to have the standard programs in biology, engineering and 'omics, but our goal is to work more of a hub-and-spoke model, to work with the best in each discipline across the country to help work together to get an answer.

My mantra is that of Andy Grove, at the time the CEO of Intel, and Andy famously said, "There's no technology that will win, technology itself will win," and I believe that.

You're not going to have the winner be genomics vs. proteomics or metabolomics or microbiomics—it's all of them together. And so the challenge is integrating them, and building models that bring in multiple technologies. So again, I view this as a team approach.

We're a small group; around the country and around the world, we have some of the greatest researchers in different disciplines. The hope is we can integrate them and work together.

MO: *Did you say that the center would be working on a database? What will that look like?*

DA: We're not creating a database, but we're going to be a repository of data. The volume we see is rather small, but we can start to pull datasets from across the world, bring them together in one place, and harmonize them and develop models.

We have a program that we develop models: just like you can see models for hurricanes off Florida, they can go route A, B or C. And after the hurricane, they'll say which model was right and why were the others wrong, and each model gets better.

We want to start to develop that in cancer. There are about several good models now, and when we start to put them in one place where people can plug in good data and say which model predicted what happened—whether it be the animal, the patient with cancer—and we can start to improve the models with this iterant feedback loops.

The Breast Cancer Research Foundation funded us for a few years to start to put together this repository of models, and we've been working with about seven groups across the world on some of these datasets. We're in conversation with others to bring them.

Obviously, now we have the resources, we're hoping to do that in a much more scaled, bigger way.

MO: *The public focus right now is on oncology bioinformatics, thanks to Vice President Joe Biden's moonshot, and many groups are working towards that data-sharing goal. Why do you think the time has come for oncology to start looking in this direction, and what*

specialty will this center bring to the table?

DA: With the convergence of electronic medical records with the convergence of more standardized data elements and data collection, data has more utility.

We're in a field now where we're starting to see some wins. There's a beautiful paper last year saying that if you're on a beta-blocker with ovarian cancer, you live longer than if you're not. Over and over, we've seen big data having impact. What you need for a field to take off is wins. We're starting to have them.

Where we can add help, and where our strength is, is in two areas: we have a fantastic group led by Carl Kesselman [division director of the Information Sciences Institute at USC Viterbi School of Engineering], who has built large databases to hold disparate data—whether it be genomic data, proteomic data, clinical trial data—start to pull them into one database. Carl and our group have really put in a paramount effort.

Second, we have a large group of modelers. There's no question, there are much better groups in the world to collect data. There are much better people who are statisticians to analyze it. What we're good at is modeling it, and so our focus is going to be creating models—go-forward models based on the data, where we can prove or disprove hypotheses. Our team has been doing that: taking various data sources and putting them together in one model set. I think that's going to be our focus.

MO: *Will you be speaking with Biden or working with his office? Do you see a potential role for the Ellison Institute in the moonshot's focus on data?*

DA: I already have. When he announced it in Davos, I was there, and we spent time together. I'll spend time with him next month. Greg Simon, who is running the program now, is a close friend.

I, like many cancer docs, was skeptical in the beginning about the moonshot program.

And then we were in Davos in January, and Biden said, "You know, my goal is not to cure cancer. It'd be great, but I don't think I will have any role in that. But if something was to take 10 years and I can make it happen in five years, I've had a major success. I want to remove hurdles and roadblocks."

That was such a mature way of looking at it. That really impressed me. We all in the field have hurdles that we know of, whether it be regulatory, IRB, collaborations with institutions or pharmaceutical companies, etc. If he can remove some of those hurdles and make it easier for us to do what we're good at, the moonshot is going to be a tremendous success.

I love now that he is taking on data—it's one of the first things—and I think it's fantastic. Obviously, our program is built on the premise of sharing data, that we're going to work with other institutions who have data and use their data and hopefully improve by harmonizing with other datasets and developing the models. Biden is removing a lot of the hurdles that we would've faced, and I applaud him and his team for that.

I wrote a piece in The New York Times two months ago about data. What I pushed for is that we have to change the attitude on data in this country. There's an attitude that "My data is private, you stay away from it, if it gets out there, I can have irreparable harm."

We have to go and push for people who use the data, who allow the data to be used for research, to be recognized as heroes. And they are part of the solution, not the problem.

I think the Biden effort will go a long way in that regard. I will play whatever role they require of me, I will support them and I'm so excited that we have powerful people in Washington who get it, who are behind this.

MO: *Are there any academic partners? Will this be an USC-centric effort, or will the Ellison Institute be recruiting or partnering with researchers and oncologists across the U.S.?*

DA: We are partnering with oncology centers across the world. We now have multiple existing collaborations that will hopefully continue to grow and get new ones.

Our goal is not to reinvent anything. If somebody is doing something well, we want to work with them. We have too much duplication in the field of cancer in this country. If everybody is good at something and we all work together, we're going to get big advances.

It's a lot easier and more efficient to get progress if I collaborate with people, than if I bring them in. If I can bring somebody in as a collaborator and give them an appointment, literally overnight—the whole notion of having to go through a year of university reviewing them—we restructured this on purpose to allow those almost instant collaborations.

MO: *It sounds like you're integrating a number of existing programs across departments into the center; is that accurate?*

DA: Yes. I'm a believer in people, not departments. It's getting people in different disciplines and bringing them into one place. To me, it's human capital that will win against cancer, not institutions or dollars or programs. It's individuals with very smart ideas.

MO: *Are there industry partnerships in the works?*

DA: We work with a number of technology providers to work with their technology and to integrate

it into the fields of cancer research and cancer care. We push a number of technology companies to innovate newer technologies that we need. I don't want to push an individual technology or company, but we're certainly good at leveraging. We have multiple technology partners now—what I want to be is to push them and say, "You're going to win here, but we're going to help you make your technology better or find a new indication and then you win."

MO: *What is the business model for sustaining the center's activities beyond the initial $200 million investment?*

DA: NIH grants, foundation grants, philanthropy, all of those will help. Every project that we do, the criteria are that it has to be able to be translated to patients very quickly.

Those in general are relatively easy projects to get funding for. We're lucky in that regard. The funding climate now is definitely pushed more to the translational side. The basic scientists have more difficulty in the current funding climate—I understand their pain and suffering right now—but the translational cancer field is a little bit easier.

MO: *What's an example of promising, translatable research going on now at USC that the center will be able to leverage?*

DA: There's a paper that came out earlier last year where they look at the eyelids of patients. The eyelid is the one spot on the body where you don't put sunscreen. When they looked at the eyelid, they found many of the DNA mutations associated with cancer from the UV radiation, yet the patients didn't have cancer.

What we've learned is that DNA mutations are necessary for cancer, but not sufficient. You need a receptive environment. One of the challenges is developing data elements to describe environments. So one of our biggest programs and I think one of the contributions that hopefully we can make in the near term are to create data elements that describe the environment.

How do you say that which environment is receptive vs. not for this cancer or that cancer on a personalized basis? Our modelers, our statisticians, our mathematicians, our physicists have worked together to try to develop data elements to describe that system which is us. It's pretty cool.

MO: *Will the center be working with others beyond the academic cancer center realm, including federal entities like NCI and NIH?*

DA: We have significant collaborations with the NCI, we have big programs with the National Health Service in the UK.

These are staggering assets with remarkable people to work with. They've been anywhere from just giving us advice to actual formal collaborations. They're a big part of what we do.

MO: *Where do you see the Ellison Institute in say, five or 10 years? When you look back, what will be the difference you hope the institute will have made?*

DA: My dream is that every patient with cancer, when they're diagnosed, we can take their information, their data elements, and put them into a model. And that model will tell us what will be the natural history of the cancer.

It will tell us what they will or won't respond to, instead of right now where we're kind of doing it based on simple characteristics—this is an estrogen-positive breast cancer, therefore we do x or y. We have to evolve to be more fine-grained in how we approach clinical decisions.

I think our big contribution will to be to develop these models so we can plug data in and start to know answers. We're privileged in that, literally, labs across the world are generating the data that will make these models work. So it's not the if-we-will-develop-it-here approach, but everybody works on it and we're going to pull it together and create these models.

This is not a case where a researcher gets a big gift and he's set for life, he doesn't have to apply for grants. The pressure has been put on us by one of the strongest, most powerful, smartest people in the world, saying, "Make a difference soon."

So I sleep less now that we have this gift than before, because this is a burden on our shoulders—and the burden is to make a difference.

I, like every cancer doctor that reads The Cancer Letter—there's very little media that focuses on this in a critical way, you do, and I love that. I see the pain and suffering on a daily basis because of this horrible disease.

That's what motivates all of us to work, and that's why we get the small amount of sleep we do, that's why we worry and think about this issue every day. We have to do better.

Slamming the Door

Part XII: More Scientists Walk Out

(Continued from page 1)

Maybe the place will become functional someday, but only the oversight committee is sent packing and after the Gogolesque characters are kicked out of CPRIT's offices in Austin. Until that occurred, an effort to rebuild would require CPRIT to turn to the scientific establishment on some other planet.

Politicians who ran CPRIT didn't seem to understand this. They continued to act as though they were going to win the war against those intellectuals.

I knew that CPRIT operatives were trying to recruit Raymond DuBois to take over after Al Gilman. That made sense for them, but not necessarily for DuBois.

With America's premier scientists leaving CPRIT publically, Texas politicians needed a scientist who had a national name and a reputation for integrity. I could also see why DuBois would talk with these people. He is polite.

But he had already agreed to accept a job at the BioDesign Institute at Arizona State. How would it be okay to run a Texas state funding agency by a part-time employee out of Arizona? Would he want to work two jobs? Most importantly, the problems at CPRIT now boiled down to matters of principle: political meddling with peer review. Gilman's entire cadre of scientists—all or nearly all of them—were about to walk out.

Why would DuBois want to get on the wrong side of *that*?

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The letters of resignation kept arriving.

The stature of rank-and-file reviewers is perhaps the most remarkable aspect of the peer review structure Gilman constructed. Now, these reviewers are sending in their letters of resignation.

None of these people really had to resign. They left because they *wanted to*, and many of them sent their letters of resignation to CPRIT officials, with a cc: to The Cancer Letter. They wanted to join Gilman on the dais for the teachable moment. It was all the more extraordinary, because scientists as a group don't like to go out of their way to make enemies.

I've seen many of my friends keep a straight face while former NCI Director Andrew von Eschenbach was expounding on his pledge to eliminate suffering and death due to cancer by 2015. Here, the scientists were jumping at the opportunity to declare that they would not accept political meddling. The Nobel laureate's experiment was producing a show of solidarity of the magnitude you don't usually see in the U.S. Scientists were acting in a manner you would expect from advocates.

Here are some of these letters:

Brian Dynlacht, *professor of pathology at the New York University School of Medicine:*

I am writing to formally resign my position as a scientific reviewer for the CPRIT Basic Science Cancer Research Committee-3, BCRC-3, effective immediately.

By way of introduction, I have been a scientific reviewer for the CPRIT BCRC-3 committee under the chairmanship of Dr. Charles Sherr. I have followed with much interest and, I must admit, substantial consternation, the series of events that have transpired at CPRIT over the past six months.

I am extremely disappointed by what I have heard, and especially upset by both accusations against Al Gilman and the direction of CPRIT leadership has chosen, which is apparently to promote commercialization at the expense of rigorous scientific review.

In all of my years in academia, I have never encountered two more honest, intellectually rigorous scientists than Al Gilman and Charles Sherr. I can say with complete certainty that their motives are, and always have been, completely free of bias.

They are the absolute cream of the crop. I wholeheartedly agree with their stance on matters that have recently surfaced at CPRIT, in particular, those matters stipulated in Dr. Sherr's resignation letter, which I will not reiterate here. On that basis, I must follow them by submitting my resignation. I anticipate that you will be receiving an onslaught of letters similar in content and sentiment to my letter.

In addition, I will forward this letter to Dr. Sherr, CPRIT review Council members, and, in all likelihood, The Cancer Letter and The Houston Chronicle.

I have served on many federal and private scientific review committees, and I have never served with such an accomplished and outstanding group of scientists. The elite panel assembled by Dr. Sherr was intellectually rigorous, honest, and conscientious. Al Gilman oversaw each meeting with professionalism beyond reproach. You will not find a better group of human beings or scientists no matter how hard you search. Let me repeat that: Drs. Gilman and Sherr

have done something remarkable here, by assembling this group, and it is unlikely that you will be able to reproduce their accomplishments without them no matter how hard you try.

You may find that it was not worth subverting the entire scientific enterprise—and my understanding was that the intended goal of CPRIT was to fund the best cancer research in Texas—on account of this ostensibly new, politically-driven, commercialization-based mission.

Indeed, I am of the opinion that such a policy—wherein science that is judged meritorious by a highly esteemed group of scientists is discounted at the expense of science that has not been methodically reviewed--will not only fail to recognize and extract the best possible science from your state, but it will in fact succumb to mediocrity and systematic abuses.

It has been an honor to serve on this esteemed committee. It is a shame that it will be completely dismantled. While it was challenging and arduous work, it was indeed a genuine pleasure to work with this group of enlightened and brilliant scientists. It is extremely unlikely that I will serve with a better group of scientists in the future.

Monica Bertagnolli, *professor of surgery at Harvard Medical School, chief of the DF/BWCC Division of Surgical Oncology, and group chair of the Alliance for Clinical Trials in Oncology:*

I am writing to inform you of my decision to resign from my position on the CPRIT scientific review panel led by William Kaelin, MD, effective Oct. 12, 2012. I do so with regret, as my work on the panel provided me with tremendous professional satisfaction.

It was a great honor to work under the direction of Dr. Kaelin, whose grasp of basic and translational cancer research is truly remarkable. He led the committee to recognize and reward excellence where it was demonstrated, and to provide constructive feedback and encouragement to researchers whose proposals were not recommended for funding.

Working with Dr. Al Gilman was one of the highlights of my professional career. His is not only one of the greatest scientists of our age, he also is one of the rare individuals who understand the real world strategies that must be employed to achieve success. In their service to CPRIT, both Dr. Kaelin and Dr. Gilman demonstrated the highest professional and ethical standards without exception, and their single goal was to serve the citizens of Texas by promoting cancer research of the best possible scientific quality and integrity.

The implication that reviews were biased toward or against a particular awardee institution is simply ridiculous. In fact, the committee ignored mention of the institution unless there was a specific reason to consider it, e.g., if the research required access to a specific resource that was only available in a particular location. It is similarly outrageous to consider that many detailed applications so painstakingly prepared by Texas researchers could be reviewed and approved for funding in good faith, only to have this review negated by diverting funding to a briefly outlined "commercialization" proposal from MD Anderson/Rice.

This shows an appalling lack of respect for the applicants as well as the reviewers. Finally, in awarding funding, I believe that it is critically important for commercialization potential to be secondary at all times to scientific quality. Many projects that have significant commercialization potential in the short term also lack scientific validity.

Without placing scientific rigor above all else, the citizens of Texas risk supporting investments that ultimately prove wasteful, while diverting resources from important work that can improve the lives of cancer patients.

My experience on the committee was one of hard work, thoughtful deliberation, and respect for the goals set forth by CPRIT. Our committee reviewed a large number of outstanding proposals from Texas cancer researchers, and I am confident that those recommended for funding will benefit the state by achieving significant advances in the battle against cancer. Unfortunately, given the events of the past several months, I can no longer be certain that this will be the case going forward.

I therefore respectfully submit my resignation.

John Cleveland, *professor and chair in the Department of Cancer Biology at the Scripps Research Institute:*

I hereby tender my resignation as a Member of the CPRIT BCRC-3A Review Panel. This decision is based on the recent events that have unfolded at CPRIT, which appear to have driven by very misguided perceptions, special interests and agendas of the Oversight Committee that, very sadly, undermined the principles of grant peer-review.

I assure you that, under the leadership of our esteemed Chair, Dr. Charles Sherr, and that of Dr. Al Gilman, the very highest principles and standards were

applied to the review of all IIRA, HIHR and MIRA grants, and that all funding decisions were made purely on the basis of the merit of the proposed science, and on their importance to the stated mission of CPRIT.

Indeed, the rigor of these reviews, and the incredible group of scientists that were recruited by Dr. Sherr, made the CPRIT BCRC-3 Review Panel truly exceptional.

It was a true honor and privilege to serve on the CPRIT BCRC-3A Review Panel, and to provide these important services to the citizens of the great state of Texas for such a worthy cause. However, given the actions of the Oversight Committee I cannot in good conscience continue to serve as a reviewer for CPRIT.

I sincerely hope that in some way this action prompts the Oversight Committee to reconsider their current direction and restore sanctity to the proper review of CPRIT applications.

William Hahn, *deputy chief scientific officer and chief of the division of molecular & cellular oncology at Dana-Farber Cancer Institute:*

I write to inform you that I am resigning from the BCRC-1A Review Panel of the Cancer Prevention and Research Institute of Texas (CPRIT) effective immediately.

When I was asked to join this committee three years ago, I did so with enthusiasm for a program that I believed had real potential to accelerate cancer research and to eventually bring new treatments to patients. The citizens and legislature of Texas are to be applauded for

their foresight and generosity to establish CPRIT as a bold statement of what can be done to improve the lives of patients affected by cancer.

For the past three years, I thoroughly enjoyed working with top cancer scientists from around the country to provide CPRIT with rigorous and impartial review to ensure that these public funds would be allocated to those projects most likely to impact the prevention, diagnosis and/or treatment of cancer.

These deliberations occurred in an environment created by Dr. Al Gilman and the chairs of the CPRIT review panels that was entirely free of political influence or institutional bias. I have served on numerous international and national study sections and can say with confidence that these CPRIT panels were models for high quality, unbiased review.

Unfortunately, recent actions of the CPRIT Oversight Committee now undermine the basic tenets of this process. The accusation that applications were ranked by institutional bias rather than scientific merit is simply not correct and is an affront to all of us who participated in these reviews. At the same time, delaying the funding of highly ranked applications to fund incubator projects without scientific review emasculates the credibility of CPRIT and the entire review process.

Moreover, I am troubled by the Oversight Committee's recent request that those of us that participated in the scientific review of commercialization applications reconsider our scoring in the absence of any additional substantive information or progress by the applicants to strengthen what were wholly naïve and underdeveloped applications.

These actions make it clear that the CPRIT Oversight Committee has elected to disregard scientific review to pursue a different agenda.

Under these circumstances, I cannot continue to serve on this panel. The Texans who made CPRIT possible deserve an unbiased process that ensures that these funds are allocated based on merit. I still believe in the potential of CPRIT and would consider serving again in the future but only if the CPRIT Oversight Committee commits to the principles of scientific rigor, intellectual integrity and impartiality that formed the basis of these original peer review panels.

If CPRIT Oversight Committee elects to bypass peer review, I fear that this will not only damage CPRIT's reputation but may also erode the public's confidence in cancer research.

J. Wade Harper, *the Vallee Professor of Molecular Pathology at the Harvard Medical School Department of Cell Biology:*

This letter is written to tender my resignation as a member of the CPRIT Basic Science Cancer Research Committee-3 (BCRC-3), effective immediately.

Having spent 15 years as a faculty member at Baylor College of Medicine and a resident of Houston, I was very excited to be asked by Dr. Sherr to participate in his review panel. This was especially the case because I have admired Dr. Sherr's science and intellect for more than 2 decades.

Recognizing that Texas institutions have significant promise, I felt that the CPRIT model and the funds available would truly be transformative, but only if the best science was funded.

I was strengthened in this feeling of promise upon the first meeting of the BCRC-3 study section, where I discovered just how scientifically stellar the BCRC-3 study section actually was. Through Dr. Sherr's vision, he was able to establish a national panel of experts who

judged each application based solely on the science and the ability of that science to transform cancer treatment in Texas.

I have served on numerous other study sections, including NIH. The BCRC-3 study section was by far the most rigorous and fair study section I have ever been associated with. This is due in no small part to Dr. Sherr's efforts in bringing this incredible group together and keeping us together for 3 years.

Having talked to members of the other scientific review panels, I believe that they all feel this way about their individual groups. Prior to joining CPRIT's review panel, I had not had the pleasure of knowing Dr. Gilman.

Through the 3 years I have known him, I have NEVER heard him say anything that would sway reviewers in either direction toward ANY grant. I have never seen him display favoritism in any form.

Thus, one of the most depressing things about the last 6 months has been the extent to which Dr. Gilman's integrity has been challenged. He has my utmost respect. Also, I must say that the new policy of having a monitor present during our discussions is one of the most insulting things that have happened to me in my professional career.

In my view, the direction that CPRIT is going—putting commercialization schemes in place at the expense of well-grounded scientific studies—will ultimately degrade the process that CPRIT originally intended.

Without appropriate and rigorous scientific review, those with the greatest hype, rather than the greatest science, will likely receive the lion's share of the funding, often I fear, with an outcome that is not in the best interest of the residents of Texas.

There is much more of a chance, using this mechanism, for favoritism to be given, and for politics to be inserted into the process. I am very much afraid that the enormous efforts that all of the study sections have given to the review process with the hope of transforming cancer research in Texas during the last three years will possibly be for naught if strict and rigorous scientific review is not maintained.

Given the dramatic changes in the approach being taken by CPRIT, I am unable to continue my support for this endeavor.

Kurt Zinn, *professor in the Departments of Radiology, Medicine and Pathology, and director of the Division of Advanced Medical Imaging Research at the University of Alabama at Birmingham:*

Thank you for the opportunity to serve as an external reviewer for the CPRIT program. I now inform you of my resignation as reviewer for the Interfaces Review Committee. I fully support Dr. Gilman and Dr. Gambhir in the positions they have taken against those in the CPRIT organization that decided to bypass scientific peer review for certain commercialization projects.

Commercialization projects should be scientifically sound if they are to be funded, and how would that be determined if the projects are steered to bypass the peer review mechanism?

As you know, I was one of the reviewers that you specifically requested for a "second look" for a commercialization project that I scored not fundable on the original review. You did not inform me that Dr. Gilman had rejected your idea to contact reviewers for a "second look." My "second look" showed the project was not different from my first review, and therefore my score was not changed.

However, upon further reflection, I think it was inappropriate for you to request a "second look" when Dr. Gilman rejected your plan. I think your style of making "on the fly" decisions during the review process is not transparent or fair to all applicants.

Eric Fearon, *the Emanuel N. Maisel Professor of Oncology, a professor in the Departments of Internal Medicine, Human Genetics and Pathology, chief of the Division of Molecular Medicine & Genetics, and associate director for basic science and deputy director of the University of Michigan Comprehensive Cancer Center:*

I am writing to offer my resignation as a member of the CPRIT Basic Science Cancer Research Committee-3 (BCRC-3), effective immediately.

The citizens of Texas and the Texas legislature are to be congratulated for their wisdom in supporting innovative cancer research and prevention efforts via the founding and funding of CPRIT. It was a great honor and privilege to serve over the past three years as a member of the BCRC-3 panel, in a scientific review process conceived by outstanding leaders such as Al Gilman, Phil Sharp, and the Cancer Research Committee chairs, alongside truly outstanding and committed cancer researchers from outside the state of Texas.

Our panel evaluated and discussed all scientific applications before the Committee without any bias or conflict of interest, with the singular goal of identifying only the most promising, innovative, and high impact

cancer research proposals.

Having participated as a panel member and/or chair at numerous scientific review committees at the NIH and multiple foundations over the past two decades, the quality of the scientific review process at the BCRC-3 panel was the most outstanding of any such evaluative process that I can recall.

Based on my reading of news articles over the past few months in various forums (e.g., Houston Chronicle, Dallas Morning News) and opinion pieces (e.g., the June 29, 2012 Houston Chronicle piece from Charles W Tate, chairman and founding partner of Capital Royalty LP, a leading investment firm focused on providing growth capital to the biopharma industry and a member of CPRIT's Oversight Committee, who chairs its Economic Development and Commercialization Subcommittee) discussing CPRIT's likely intentions going forward, I am left with the impression that "grand" science and "commercialization" projects may represent much of the future for CPRIT.

As a result, I am uncertain that the robust scientific review process for CPRIT applications of all types that was conceived by Drs. Gilman, Sharp and the other review panel chairs, and executed by the varied review panels will be needed going forward. Indeed, I found the press release from CPRIT on their website (Sept. 21, 2012) stating that "we look forward to continuing and expanding our support for MD Anderson's prevention, research and commercialization projects, particularly the multidisciplinary groups of researchers and clinicians that are mounting comprehensive attacks on the eight target cancers" to be a most remarkable statement, especially so, in light of the fact that the statement is a forward-looking one.

To me, the CPRIT press release seems to imply that certain, yet-to-be-submitted MD Anderson applications to CPRIT have already been judged to be sufficiently meritorious to deserve CPRIT support, even though the hypothetical applications have presumably not yet been fully conceived or submitted in final version to CPRIT by MD Anderson scientists and clinicians, nor have the hypothetical applications been subjected to full scientific evaluation by outside, independent review panels.

Perhaps for some in the cancer research field such as myself, the CPRIT press release statement on their website could be seen as consistent with the view that unencumbered and unbiased expert peer-review of cancer research applications submitted to CPRIT might simply be a quaint relic of the past.

Scott Kern, *associate professor of oncology and pathology at Johns Hopkins University Sidney Kimmel Comprehensive Cancer Center:*

It is ironic that I again find myself in the undesirable position of resigning from a hard-working and highest-quality scientific study section. As Twain noted, history does not repeat itself, but it does rhyme.

Ten years ago, I served on the scientific review board of a private philanthropic organization. In an unusual development, I was asked to review two special grant applications that had arrived out-of-cycle.

After my review, I was informed by the organization that they had beforehand decided to fund the two grants, a decision made prior to obtaining the reviews from the scientific board.

They had in this instance perhaps operated as a direct money conduit and not as a peer review-guided granting operation.

Owing to the deprecated role of scientific review under such procedures, I regretfully

resigned from their board. To my knowledge, subsequently they adhered tightly to the procedures established in their founding document, pursued a stellar and constructive path, and remain a healthy organization.

I now find that a somewhat similar situation exists at CPRIT.

The irony is as follows. The PI of a grant receiving questionable dispensation ten years ago, and a PI of a grant recently under critical scrutiny for improper dispensation at CPRIT, were the identical person.

For history to rhyme,

I must resign.

I wish CPRIT well.

Gregory Longmore, *director of the Section of Molecular Oncology at Washington University in St. Louis:*

I am writing to inform you that I am resigning my position as member of the CPRIT Basic Science Cancer Research Committee-3 (BCRC-3), effective immediately.

Carolyn Anderson, *professor of radiology and pharmacology & chemical biology, and director of the Molecular Imaging Laboratory at the University of Pittsburgh:*

This e-mail is to inform you of my resignation, effective immediately, as a reviewer for CPRIT Interfaces Review Committee.

I thoroughly enjoyed working with outstanding

scientists on the review panel, as well as our esteemed chair, Dr. Gambhir.

I am also privileged to have had the opportunity to work with Dr. Al Gilman, who was incredibly supportive of the peer review process and of all the reviewers, which lead to the funding of outstanding cancer research in the state of Texas.

Working with consummate professionals such as JoAnn Eckert and the SRA staff, especially Rajan Munshi, made the experience of reviewing for CPRIT feel a pleasure more than hard work.

I sincerely hope that the unfortunate circumstances that have led to the numerous resignations of the council leaders and reviewers can be rectified.

CPRIT has done the field of cancer research and cancer patients in Texas a tremendous service, and hopefully this can continue in an honorable fashion that abides by the principles of scientific peer review.

NIH Makes Sweeping Changes In Clinical Center Governance

The NIH Clinical Center will be placed under a new system of governance, similar to that of hospitals.

Replacing Director John Gallin and the current management structure, NIH has begun "the process of changing the leadership structure of the Clinical Center to model those of world class hospitals in the United States," institute officials said in a statement.

"NIH will begin a nationwide search for a physician CEO with proven experience in management of a complex inpatient and outpatient facility," the statement reads. "This individual will be ultimately responsible for oversight of all facilities and will report quarterly to the new Hospital Board, providing metrics about hospital performance and regulatory compliance."

Gallin, who has served as director of the clinical center for the past 22 years, will remain at the center for the near future, implementing the recommendations of a report by an outside group.

Gallin and his team "will continue their leadership of the Clinical Center, including working to implement the Red Team recommendations," the NIH statement reads. "NIH is deeply grateful to Dr. Gallin and his colleagues for their dedicated leadership, and will count on them over the next few months to move this effort forward with maximum energy and intensity."

The working group's report said that "failing to take appropriate steps to minimize [research] risks is a disservice to both the patients and the quality of the research itself" and found "substantial operations issues," including:

• "Absence of a readily apparent and anonymous avenue to escalate concerns within NIH beyond immediate supervisors,

• "Failure of supervisors to appropriately address and escalate important deficiencies that were reported by staff,

• "Evolution of a culture and practice in which patient safety gradually, and unintentionally, became subservient to research demands,

• "Insufficient expertise in regulatory affairs, compounded by misunderstandings about how to comply with regulations for a federal research institution conducting clinical operations,

• "Fragmentation of authority and responsibility for clinical operations, driven by a unique decentralized structure, authority, and funding for intramural clinical research, resulting in accountability and quality assurance gaps that could compromise patient safety,

• "Inadequate independent oversight of safety and regulatory compliance within NIH,

• "Insufficient regular monitoring and metrics for identifying and tracking needed steps for improvement."

ACS Report Assesses Progress In 25-Year Goal Against Mortality

The American Cancer Society published a report assessing the progress made in its 25-year goal to reduce cancer death rates by 50 percent. The report finds areas where progress was substantial, and others where it was not.

The report, appearing in the ACS journal CA: A Cancer Journal for Clinicians, said the best improvements were seen in cancers for which prevention, early detection, and treatment tools are available, including cancers of the lung, colon, breast, and prostate.

In 1996, the Board of Directors of the American Cancer Society set a goal to reduce what looked to be peak cancer mortality in 1990 by 50 percent by the year 2015. The current analysis, led by Tim Byers of the University of Colorado, examined trends in cancer mortality across the 25-year challenge period. The rates for 2015 were estimated as a linear extrapolation of the trends from 2010 to 2014.

The report found:

• In 2015, the overall cancer death rate was 26 percent lower than in 1990—32 percent lower among men and 22 percent lower among women.

• Among men, mortality rates dropped for lung cancer by 45 percent, for colorectal cancer by 47 percent, and for prostate cancer by 53 percent.

• Among women, mortality rates dropped for lung cancer by 8 percent, for colorectal cancer by 44 percent, and for breast cancer by 39 percent.

• Declines in the death rates of all other cancer sites were substantially smaller—13 percent among men and 17 percent among women.

• Major factors included progress in tobacco control and improvements in early detection and treatment.

"As we embark on new national cancer goals, this recent past experience should teach us that curing the cancer problem will require 2 sets of actions: making new discoveries in cancer therapeutics and more completely applying those discoveries in cancer prevention we have already made," wrote the authors.

The report says not fully reaching the goal should be seen as an opportunity. "That the ACS challenge goal to reduce US cancer mortality by 50 percent over the 25-year period from 1990 to 2015 was only one-half achieved should be seen as a glass half full. This progress should eliminate any historical remnants of cancer fatalism, and it should now stimulate our national imagination about what might be possible to achieve into the future."

The report says the effort also has a valuable lesson in goal-setting: "The best goals are those that stretch the limits of what might actually be achieved by renewed efforts. There is a sweet spot in goal setting between projecting what will likely happen regardless of renewed efforts (setting the bar too low) and creating unrealistic challenges that tend to paralyze us (setting the bar too high)."

The report concludes: "All sectors of civil society will need to join in efforts to further reduce cancer mortality in the United States, including those focused on the many social determinants of cancer, including income, availability of care, and many other social and environmental factors impacting cancer-reducing policies and programs. How much more progress we will make will depend on the extent to which policy makers and the American public can join together to create systems and incentives to understand cancer better, to reduce several of the known risk factors for cancer, to better diagnose cancer earlier, and to assure that state-of-the-art treatment is available for all."

In Brief

Brigham Does Not Contest Plaintiffs' Offers of Proof as Morcellation Cases Proceed

BRIGHAM & WOMEN'S HOSPITAL chose not to contest the plaintiffs' offers of proof in two medical malpractice lawsuits against the Boston hospital at a Massachusetts tribunal May 13.

The two lawsuits related to power morcellation will now be allowed to proceed. The suits were filed by Richard Kaitz and Hooman Noorchashm, whose wives, Erica Kaitz and Amy Reed, had the controversial minimally invasive surgery at Brigham in 2012 and 2013, respectively.

The procedure, which until recently was performed in an estimated 100,000 women annually in the U.S., is the focal point of a two-year debate that has divided the surgical field. When a previously undiagnosed malignant tumor—usually a sarcoma—is present, the procedure spreads the cancerous tissue, upstaging the disease (The Cancer Letter, How Medical Devices Do Harm).

Erica died Dec. 7, 2013 from metastatic leiomyosarcoma, and Reed, formerly an anesthesiologist at Beth Israel Deaconess Medical Center, is undergoing treatment for stage IV disease.

"It's a rare case that the defendant does not contest the plaintiff's offer of proof at the tribunal stage," said Tom Greene, the attorney representing Kaitz and Noorchashm's families. Brigham did not respond to an email from The Cancer Letter by deadline.

Massachusetts law requires that a tribunal—consisting of a judge, an attorney, and a physician—review medical malpractice cases to screen out lawsuits that are not supported by clinical evidence or fact. The process determines whether there is sufficient evidence for the case to proceed.

According to the Massachusetts Medical Society, tribunals screen out approximately 16 percent of all medical malpractice cases in the state.

THE AMERICAN UROLOGICAL ASSOCIATION honored its 2016 award recipients during its 111th Annual Meeting in San Diego.

William Marston Linehan received the Ramon Guiteras Award for his contributions to the art and science of urology, most notably in the identification of genes associated with different types of kidney cancers and developing new strategies for their management.

Margaret Sue Pearle was presented with the Hugh Hampton Young Award for contributions to the science of nephrolithiasis by providing the evidence base that has shaped paradigms for the medical prevention and surgical therapy of stone disease, and for exemplary service in AUA Education and Guidelines.

Benjamin Canales received the Gold Cystoscope Award for his research initiatives in the pathogenesis of nephrolithiasis, which include the development of new animal models and the exploration for novel therapeutic approaches. The Gold Cystoscope Award is presented to a urologist within 10 years of completing residency training.

James Montie received the Lifetime Achievement Award his leadership in the field of urologic oncology and a lifelong commitment in helping advance urological education.

Peter Albertsen received the Eugene Fuller Triennial Prostate Award for his contributions to the understanding of prostate cancer, most notably in epidemiology and statistical analysis. This award is presented once every three years for contribution to the study of the prostate gland and its associated diseases.

W. Hardy Hendren III received the Victor A. Politano Award for his contributions in developing surgical techniques of reconstruction of urogenital anomalies and undiversion in children. This award is for research and work in the field of incontinence and for enhancing the treatment of incontinent patients and improving quality of life.

William Parry was presented with the William P. Didusch Art and History Award for his work in preserving the art and history of urology, naming the William P. Didusch Urology History Museum and creating four award winning urology exhibits. This award recognizes contributions to urological art, including, but not limited to, illustrations, sculpture, still photography, motion pictures and television productions.

Paul Lange received the Gold Cane Award for his career of academic leadership, mentorship and innovative contributions to the fields of urological oncology and endourology.

Medivation Inc. received the Health Science Award for support of physician and patient education in prostate cancer.

The Distinguished Contribution Awards are presented to individuals who have made contributions to the science and practice of urology, including, but not limited to, contributions made in a sub-specialty area, for military career service or for humanitarian efforts. The following individuals were recognized with this award:

• **Gopal Badlani**, for leadership as secretary of the American Urological Association as well as decades of urological education and humanitarian service.

• **Allen Morey**, for contributions to the science and education of civilian and military urologists in the performance of urological reconstructive surgery as well as 18 years of philanthropic missions to Honduras.

• **Peter Schlegel**, for years of research, discovery and treatment of male infertility as well as urological education and dedication to students, residents and fellows.

The Distinguished Service Awards are presented to individuals who have made contributions to the goals of the AUA. The following individuals received this award:

• **Martin Dineen**, for more than two decades of leadership in health policy as well as humanitarian service in Haiti to eliminate urogenital elephantiasis.

• **Roger Dmochowski**, for leadership in the specialty of Female Pelvic Medicine and Reconstruction, and for development of AUA Guidelines.

• **Raju Thomas**, for leadership as the chair of urology at Tulane University, particularly after the devastation of Hurricane Katrina, as well as for humanitarian service in providing minimally invasive surgery to less-privileged areas of the world.

Presidential Citations are presented to individuals deemed to have significantly promoted the cause of urology during a specific period of time. Each recipient is chosen by the AUA president. Presidential Citations were bestowed upon the following individuals:

• **Arnold Belker**, for years of leadership in andrology and reproductive medicine and for innovation and teaching in microsurgery.

• **Peter Bretan**, for leadership in disaster relief and humanitarian work both in the U.S. and abroad; and for teaching urological skills in developing nations.

• **Anthony Casale**, for years of leadership in pediatric urology, for the treatment of complex urogenital anomalies in children and resident teaching.

• **Col. Paul Friedrichs**, for outstanding leadership in the United States Air Force Medical Corps, for support of combat operations in Iraq, and for leadership in the AMA House of Delegates.

• **J. William McRoberts**, for many years of leadership as chair of urology at the University of Kentucky and for service as the AUA Southeastern Section secretary and president.

• **Drogo Montague**, for innovation and teaching in prosthetic surgery and penile reconstruction and for leadership in creating AUA Guidelines.

TOM ANDRUS was named chief digital officer and executive vice president of the **Prostate Cancer Foundation**.

Most recently, Andrus was general manager and senior vice president of AXS.com, a division of AEG, building a new ticketing company. Previously, he was senior vice president of product at MySpace, where he led the product, design, mobile, and search businesses.

Prior to joining MySpace, Andrus spent eight years at EarthLink where he created the company's product management team, led business development, and established new divisions, launching the wireless, voice, cable and value-added services business units. He also led the Utilities product team at Symantec/ Norton, and was one of the founding employees of Fitnesoft, a health management software company.

STAND UP TO CANCER published a series of Certification for Nursing Education training modules, with the **Boston College William F. Connell School of Nursing**, focused on immunotherapy.

The first web-based CNE modules will be available in July. In its first round, the program will seek to train 25 nurses working in immunotherapy. The program was announced as part of National Nurses Week, May 6-12.

The program will address providing care for cancer patients receiving immunotherapy, including education on immunology and related pathophysiology, symptom management, and nursing interventions to reduce symptom distress and promote wellness. The modules will meet CNE standards and each module will provide 3.5 to 5 contact hours from the Boston College William F. Connell School of Nursing.

CANCERCARE published a report illustrating the physical, emotional, financial, practical and informational needs cancer patients experience during and after clinical treatment.

The 2016 **Patient Access and Engagement Report** analyzed more than 3,000 patients in ethnicity, income, education, geography, age, insurance, cancer type and treatment stage—and evaluated their understanding of their diagnosis and access to care, participation in treatment planning, communication and engagement with providers, insurance and financial issues, the impact of cancer on quality of life, and issues related to survivorship. The project was made possible by AbbVie, Amgen, AstraZeneca, Bristol-Myers Squibb, Genentech, Helsinn Therapeutics, Gilead Sciences, Incyte Corporation, Janssen Oncology, Lilly, Merck, PhRMA, and Pfizer.

The report found that people in all stages of cancer say they don't have enough information about their illness, treatment options, benefits and risks, clinical trials, insurance coverage, and how to find emotional, financial and practical support.

One-quarter of respondents ages 25 to 54 disagreed with some of their doctors' recommendations for diagnostic testing and did not follow them, with the majority citing cost as the reason. Fewer than half of respondents discussed the cost of follow-up testing with their physician. Patients ages 25 to 54 had nearly twice as many post-diagnosis conversations about their cancer with nurses, religious leaders, social workers, physician assistants, or nurse practitioners as patients 55 and older.

The report is available on the CancerCare website. www.cancercare.org/accessengagementreport

CANCER SUPPORT COMMUNITY BENJAMIN CENTER presented its annual Gilda Award Gala in Los Angeles. The organization honored actress **Frances Fisher** with the Gilda Award; CSC advocate **Joyce Green** with the Wellness Award; and City of Hope's **Matthew Loscalzo** with the Harold H. Benjamin Innovation Award.

The event was hosted by John Sencio, a national television host, producer and cancer survivor.

Loscalzo is the Liliane Elkins Professor in Supportive Care Programs, professor in the Department of Population Sciences, executive director of the Department of Supportive Care Medicine, and the administrative director of the Sheri & Les Biller Patient and Family Resource Center at the City of Hope-National Medical Center.

Fisher has starred in over 30 theatrical productions and was honored for promoting wellness and generosity. Green served as director of development for Cancer Support Community Benjamin Center.

CITY OF HOPE received a $2.3 million R01 research project grant from NCI to fund studies associated with a phase I/II clinical trial in relapsed/ refractory adult acute myeloid leukemia. The research team will be led by Steven Rosen, City of Hope's provost and chief scientific officer.

The phase II clinical trial will test 8-chloro-

adenosine in AML patients whose disease has failed to respond to initial chemotherapy. The research will also detail the drug's mechanism of action, and further characterize the cytotoxic effect of the drug on leukemia stem cells. In addition, researchers will conduct genomic profiling of AML cells to generate gene expression signatures that may help identify patients who may particularly benefit from 8-chloro-adenosine treatment.

The Rising Tide Foundation will fund the clinical trial testing the drug's safety and efficacy, while the NCI grant will fund correlative studies in genomic profiling and the drug's mechanism of action in patients.

BIODELIVERY SCIENCES INTERNATIONAL Inc. and **Collegium Pharmaceutical Inc**. signed a licensing agreement in which BDSI grants exclusive rights to develop and commercialize Onsolis (fentanyl buccal soluble film) in the U.S. to Collegium.

Onsolis is an opioid agonist indicated for the management of breakthrough pain in cancer patients 18 years of age and older who are already receiving and who are tolerant to opioid therapy for their underlying persistent cancer pain.

Under terms of the agreement, Collegium will be responsible for the manufacturing, distribution, marketing and sales of Onsolis in the U.S. Both companies will collaborate on the ongoing transfer of manufacturing, which includes submission of a Prior Approval Supplement to FDA. Upon approval of the supplement, the New Drug Application and manufacturing responsibility will be transferred to Collegium.

Financial terms of the agreement include: $2.5 million upfront non-refundable payment, payable to BDSI within 30 days; reimbursement for a pre-determined amount of the remaining expenses associated with the ongoing transfer of manufacturing of Onsolis; $4 million upon first commercial sale of Onsolis in the U.S.; and up to $17 million in potential payments based on achievement of performance and sales milestones.

THOMAS JEFFERSON UNIVERSITY joined the **TriNetX** network for clinical trial design and to support Jefferson's clinical research programs.

Pharmaceutical researchers will be able to access Jefferson's de-identified clinical data through TriNetX's network of healthcare institutions to support clinical study and protocol design, site selection, and patient recruitment across a range of therapeutic areas and development stages.

The UCLA Department of Pathology and Laboratory Medicine and **Leica Biosystems** will collaborate in digital pathology.

Product testing will be conducted with UCLA to validate digital pathology in a high-volume setting. This joint effort builds upon the existing relationship between UCLA and Leica Biosystems that was established in 2011.

The pathology team at UCLA will be working with Leica Biosystems Aperio ePathology and will test and provide quantitative feedback on current and next-generation products from bench research to full clinical adoption.

ST. JUDE CHILDREN'S RESEARCH HOSPITAL, with **Univision Local Media**, raised $4 million during this year's Promesa y Esperanza (Promise and Hope) radio event held in 17 media markets in the U.S. and Puerto Rico April 7-8.

St. Jude content included more than 30 hours of radio programming and featured several patient family stories, broadcasted coast to coast via Univision's radio network, television affiliates, network programs, websites and social media. Since the partnership began in 2006, the St. Jude/Univision national radio event has raised more than $56 million.

PHARMACEUTICAL RESEARCH AND MANUFACTURERS OF AMERICA'S member companies invested an estimated $58.8 billion in research and development in 2015, up 10.3 percent from 2014, based on the 2016 PhRMA annual member survey published in the 2016 Biopharmaceutical Research Industry Profile.

According to PhRMA, the biopharmaceutical industry is the most research-intensive sector of the U.S. economy, investing on average six times more in R&D as a percentage of sales than all other manufacturing industries.

The sector also accounted for an estimated 17 percent of all U.S. business R&D spending, the largest share of R&D spending by U.S. businesses. From 2000 to 2015, more than 550 new medicines were approved by FDA, including a record 56 new medicines in 2015.

Drugs and Targets

FDA Expands Imbruvica Label To Include CLL and SLL Patients

FDA approved an expansion to the Imbruvica (ibrutinib) prescribing information based on data supporting its use in patients with chronic lymphocytic leukemia/small lymphocytic lymphoma.

The approved label now includes overall survival data from the Phase III RESONATE-2 (PCYC-1115) trial in treatment-naïve CLL/SLL patients 65 years or older. The updated label also contains clinical data from the phase III HELIOS (CLL3001) trial investigating the use of Imbruvica in combination with bendamustine and rituximab versus placebo plus BR in patients with relapsed or refractory CLL/SLL.

Updated data from the RESONATE-2 trial reflect a statistically significant 56 percent reduction in the risk of death with Imbruvica compared to chlorambucil after a median follow-up of 28.1 months (HR=0.44 [95% CI, 0.21, 0.92]). The RESONATE-2 trial served as the basis for the March 2016 FDA approval of Imbruvica as a first-line treatment for patients with CLL.

Additionally, the first data from the HELIOS study on the use of Imbruvica in combination with other therapies were added to the label, highlighting the improvement in progression-free survival and overall response rate when using Imbruvica plus BR versus placebo plus BR in patients with relapsed/refractory CLL/SLL. Following a review of the November 2015 supplemental New Drug Application, the FDA has expanded the indication to include the use of Imbruvica for SLL patients with or without deletion of the chromosome 17p.

"The update helps to affirm the established efficacy, safety and tolerability of this therapy for the treatment of patients with CLL/SLL, both as a monotherapy or in combination with other agents," said Jan Burger, associate professor in the Department of Leukemia at MD Anderson Cancer Center, and RESONATE-2 study lead investigator.

FDA approved Lenvima (lenvatinib), Eisai's multiple receptor tyrosine kinase inhibitor, in combination with everolimus for the treatment of patients with advanced renal cell carcinoma who were previously treated with an anti-angiogenic therapy.

The approval was based on the results of a registration study, Study 205, in which the once daily combination of 18 mg Lenvima and 5 mg everolimus demonstrated a substantial improvement in progression-free survival, objective response rate and clinically meaningful overall survival when compared with everolimus alone.

"Lenvatinib plus everolimus is the first and only FDA-approved regimen that successfully combines treatments that employ tyrosine kinase and mTOR inhibition, the primary targets of advanced RCC treatment for the past decade," said Robert Motzer, of Memorial Sloan Kettering Cancer Center, and the principal investigator of the study. "This combination regimen led to enhanced efficacy and helped patients with advanced RCC live longer without disease progression or death than those treated with everolimus alone. These noteworthy findings advance the treatment paradigm for this patient population."

Lenvima was granted Breakthrough Therapy designation by the FDA for this indication, and the application received Priority Review, which is assigned to drugs the FDA believes have the potential to provide a significant improvement in the treatment of a serious condition.

In Study 205, a phase II trial, Lenvima and everolimus resulted in a median PFS nearly three times that of everolimus alone. The median PFS in patients treated with the combination (n=51) was 14.6 months (95% CI: 5.9-20.1) compared with 5.5 months (95% CI: 3.5-7.1) for those treated with everolimus alone (n=50) (HR 0.37; 95% CI: 0.22-0.62). The combination regimen resulted in a 63 percent reduction in the risk of disease progression or death compared with everolimus alone.

The objective response rate was 37 percent (95% CI: 24-52) in patients treated with the combination regimen (35% partial response + 2% complete response) compared to 6 percent (all partial response, 95% CI: 1-17) in patients treated with everolimus alone.

The patients in the combination arm experienced a 10.1-month increase in median OS compared with those who received everolimus monotherapy (25.5 months [95% CI: 16.4-32.1] versus 15.4 months [95% CI: 11.8-20.6]; HR 0.67; 95% CI: 0.42-1.08). This OS analysis was conducted when 63 percent of deaths had occurred in the combination arm and 74 percent of deaths had occurred in the everolimus arm.

Lenvima was first approved in the U.S. in February 2015, for patients with locally recurrent or metastatic, progressive, radioactive iodine-refractory differentiated thyroid cancer.

Health Canada granted approval for Imbruvica (ibrutinib), as an oral, once-daily, single-agent therapy for the treatment of patients with Waldenström's macroglobulinemia.

This approval was based on an investigator-led, multicenter, prospective, single-arm study in 63 patients who had received at least one prior therapy. The results of the study were published in the New England Journal of Medicine in 2015.

The median age of patients was 63 (range of 44-86 years old) and the median number of prior therapies was two (range of 1-11). Patients received Imbruvica 420 mg once daily. After a median duration of follow-up of 14.8 months, Imbruvica was associated with a 87.3 percent overall response rate, and a 69.8 percent major response rate. The median time for patients to achieve at least a minor response to treatment was one month. The median duration of response had not been reached.

In Canada, Imbruvica is indicated for the treatment of patients with chronic lymphocytic leukemia, including those with 17p deletion, who have received at least one prior therapy, or for the frontline treatment of patients with CLL with 17p deletion. In addition, Imbruvica was issued marketing authorization with conditions for the treatment of patients with relapsed or refractory mantle cell lymphoma, pending the results of trials to verify its clinical benefit.

Imbruvica is co-developed by Cilag GmbH International, a member of the Janssen Pharmaceutical Companies and Pharmacyclics LLC, an AbbVie company. Janssen Inc. markets Imbruvica in Canada.

Health Canada provided conditional approval of Ibrance (palbociclib) for the treatment of postmenopausal women with estrogen receptor-positive, human epidermal growth factor receptor 2-negative advanced breast cancer as initial endocrine-based therapy for metastatic disease.

The Health Canada approval of Ibrance is based on the final results of the phase II PALOMA-1/TRIO 18 trial (n=165), which studied whether Ibrance in combination with letrozole prolonged progression-free survival compared with letrozole alone in postmenopausal women with ER-positive, HER2-negative locally advanced or mBC who had not received previous systemic treatment for their advanced disease. The Health Canada approval of Ibrance is contingent upon verification and description of clinical benefit in a confirmatory trial. Ibrance is sponsored by Pfizer Canada.