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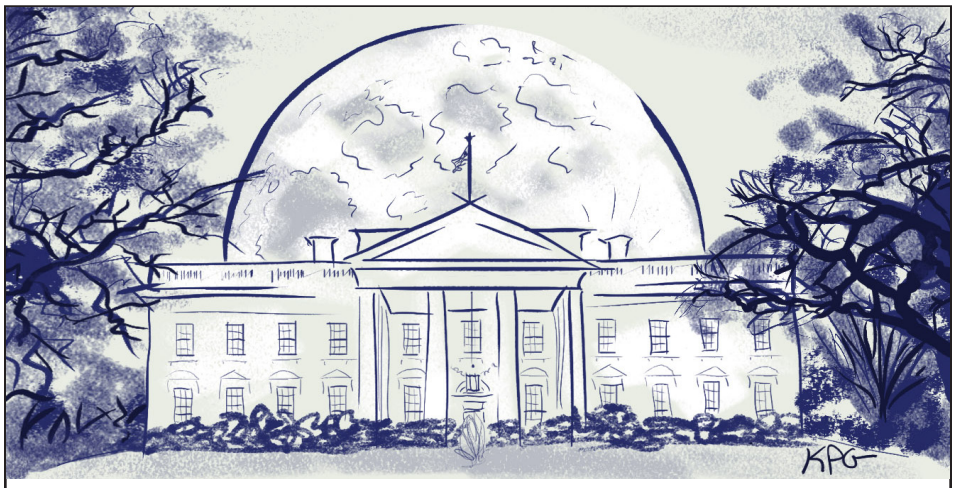

Obama's $4.1 Trillion Budget Proposes Mandatory Funds for $1 Billion Moonshot

By Matthew Bin Han Ong

President Barack Obama Feb. 8 unveiled his budget proposal for the 2017 fiscal year—a $4.1 trillion spending blueprint that is unlikely to be passed by a Republican-controlled Congress.

The administration's proposal appears to cut the NIH existing budget by $1 billion in discretionary funding and makes up the difference with mandatory funding.

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Conversation with The Cancer Letter

Sigal: FDA Should Consolidate Cancer Portfolio

President Barack Obama's Feb. 8 budget request for fiscal year 2017 slates $75 million in additional funding for FDA for the creation of a virtual Oncology Center of Excellence.

The proposal is arguably the most tangible component of Vice President Joe Biden's National Cancer Moonshot program, which aims to double progress in cancer research and drug development over the next five years.

(Continued to page 4)

Slamming the Door

Part III: 18,000 Bosses

By Paul Goldberg

Between the fall of 2011 and the spring of 2012, I watched MD Anderson from afar, and I didn't think about CPRIT at all.

Friends who attended early meetings with Ronald DePinho soon after he became MD Anderson's president said that he was literally grading presentations made to him by faculty members and administrators.

"This was a C-," he would say.

It was difficult to get a B.

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President's 2017 Budget Proposal Requests $1B for Moonshot

(Continued from page 1)

In a joint snub, the House and Senate budget committees declined to hold a hearing for Shaun Donovan, the director of the Office of Management and Budget. The move marks the first time in 41 years that Congress has refused to review a president's budget.

"It appears the President's final budget will continue to focus on new spending proposals instead of confronting our government's massive overspending and debt," said Senate Budget Committee Chairman Mike Enzi (R-Wy.) in a Feb. 4 joint statement with House Budget Committee Chairman Tom Price (R-Ga.). "It is clear that this President will not put forth the budget effort that our times and our country require. Instead of hearing from an Administration unconcerned with our $19 trillion in debt, we should focus on how to reform America's broken budget process and restore the trust of hardworking taxpayers."

Since Obama took office in 2009, annual deficits have been cut by three-quarters, to 2.5 percent of the gross domestic product, and the country's unemployment rate has gone down by more than half, to 4.9 percent.

The president's budget request, which describes spending priorities from reducing poverty to fighting Islamic State, also includes additional details on the $1 billion initiative to jumpstart the national cancer program. The moonshot proposal was announced during Obama's final State of the Union address Jan. 12. Vice President Joe Biden is leading the program, which aims to achieve a decade's worth of progress within the next five years.

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The $1 billion proposal establishes a game plan for how the funds will be spent: the moonshot initiative will begin with $195 million in cancer research at NIH in fiscal 2016, according to the White House.

The fiscal 2017 budget proposes to allocate $755 million in mandatory funds for new cancer-related research activities—$680 million for NIH and $75 million for FDA. The remaining $50 million is expected to go to the Departments of Defense and Veterans Affairs through funding Centers of Excellence.

FDA's budget would remain roughly flat in the president's request, receiving an increase just shy of 1 percent. The president also slates $4.4 million for the agency's work in the Precision Medicine Initiative—nearly twice the funds budgeted for 2016. On Feb. 9, the agency published its budget request, seeking $5.1 billion in fiscal 2017, an eight percent increase over the enacted 2016 budget.

"Funding is a perennial challenge at the FDA. This is an agency that over time has been given more and more responsibilities by Congress," said Ellen Sigal, chair and founder of Friends of Cancer Research. "The administration's moonshot increases FDA funding by $75 million, a crucial funding increase needed to implement the types of programs proposed here. The White House has said this is part of an initial investment representing a down payment on the National Cancer Moonshot."

A conversation with Sigal appears on page 1.

The White House proposes $33.1 billion for NIH in 2017, a 2.6 percent boost over current levels. This $825 million infusion includes the $680 million for Biden's moonshot, $100 million for the Precision Medicine Initiative for a total of $230 million, and $45 in new money for the BRAIN initiative.

In fiscal 2016, NIH received a $2 billion raise to $31.3 billion, and NCI's budget was increased from $4.95 billion to $5.2 billion.

Mandatory Funding for Moonshot?

The administration proposes using mandatory funds—as opposed to appropriated discretionary funds—to pay for the moonshot as well as some of the new raises for NIH, which means that lawmakers would need to establish a dedicated funding source.

For instance, the 21st Century Cures Act, an initiative passed by the House to modernize clinical trials and expedite drug development, would provide NIH with $9 billion in new money over five years by selling some of the federal government's petroleum reserve.

Oncology groups applaud the moonshot proposals,

which promise a much-needed infusion of funds for research. However, it is unclear whether Congress will honor the president's $1 billion request for the cancer moonshot program.

"The president's fiscal year 2017 budget sets an ambitious course to accelerate discovery in the fight against cancer," said Christopher Hansen, president of the American Cancer Society Cancer Action Network. "The proposed 13 percent increase for NCI would go a long way to restore funding shortfalls that have severely hampered progress in the last decade and builds on the support provided by Congress in FY16."

Over 185 state and national organizations and cancer centers issued a joint statement Feb. 9 thanking Biden for leading the moonshot program.

"We have heard your call for a greater degree of collaboration and interaction, and we are writing to express our collective ambition and enthusiasm to work with you to carry this mission forward," the groups said in the letter. "Our goal is shared—defeat all forms of cancer."

Several advocacy organizations expressed concern about the administration's proposal to cut NIH's existing budget by $1 billion from the appropriations process, and make up the difference with mandatory funding.

"One notable omission from the president's proposal, however, is a significant increase in NIH discretionary spending," said Julie Vose, president of the American Society of Clinical Oncology. "ASCO urges predictable research funding through the traditional discretionary spending process. Mandatory funding should supplement—not supplant—reliable annual increases for the NIH that at least keep pace with the rate of biomedical research inflation."

Funding increases for NIH should be consistent, United for Medical Research said in a statement.

"While we appreciate that President Obama's overall goal is to increase funding for biomedical research, we are disappointed his proposed budget would actually decrease the baseline funding level for the NIH in FY2017," UMR said. "We commend the president's inclusion of funding to support cancer-related research activities for the recently launched moonshot initiative, however, UMR believes that both strong annual appropriations plus the use of mandatory funding are needed to put the NIH back on a sustainable growth path."

The president's budget also proposes cuts to Medicare payments for cancer drugs, reducing payment by half to Average Sales Price plus 3 percent as a cost savings measure.

Critics say that the proposed cut would actually reduce payments to a little above ASP, considering that the Centers for Medicare and Medicaid Services has already reduced payments from ASP+6 percent to ASP+4 percent, when it applied sequestration cuts to the cost of cancer drugs.

"These cuts to cancer care increase costs to patients and handicap community cancer practices that are the primary participants in vital clinical trials," said Bruce Gould, president of Community Oncology Alliance and a practicing community oncologist with Northwest Georgia Oncology Centers in Marietta, Ga. "The president calls for a moonshot on cancer, but his budget, with misguided cuts and insufficient research funding, scuttles the rocket before it even gets to the launch pad."

ASCO is concerned about some aspects of Obama's proposal that would "undermine" the goals of the moonshot program, Vose said.

"Proposals to withdraw resources from the cancer care delivery system by reducing drug payments, specifically from 106 percent to 103 percent of average sales price—without overall payment reform—will jeopardize the very system needed to deliver on the promise of science," Vose said. "ASCO will continue to work closely with Vice President Joe Biden, who is leading the National Cancer Moonshot initiative, and with members of Congress as they commence the budget and appropriations process.

"We urge Congress to build on last year's bipartisan support for federal research by providing FY 2017 funding levels that will speed advances in cancer prevention, diagnosis and treatment—and will reduce the human suffering and loss of life that cancer inflicts on millions of Americans each year."

Biden: The "Profit Motive" of Data Sharing

Speaking at Duke University Feb. 10, Biden focused on data sharing, describing his astonishment at the way cancer organizations are building separate, and potentially duplicative bioinformatics databases.

Following is an excerpt of Biden's remarks:

We have to figure out a way to share information more. I'd like to focus on Big Data. I think as an outsider looking in, trying to become as informed as I possibly can, the greatest hope lies in the aggregating of enormous amounts of data that exist out there already. And a few years ago, it took more than a decade and $3 billion to sequence the human genome—the head of NIH [Francis Collins] was one of the leaders in that effort—and it now takes less than a day and costs about $1,500.

But it's spread all over the world: a piece of data is at Duke, another at MD Anderson, pieces are at other institutions. Imagine if we could collocate that information; imagine if we had full access in one form of the Utah population data, imagine what could happen.

I met with four incredibly competent, advanced groups that have put themselves together—leading cancer institutions, SAP's involved, Oracle—and I listened to them, and they're all doing the same thing. They're all about to spend hundreds of millions of dollars, well over $1 billion, for them to have their own data collection.

And I asked them all whether they'd be willing to meet with me alone in a room in the vice president's residence to answer the question, 'Why?' No, I'm not being facetious! I'm being deadly earnest about this. I understand the way the system is built, and there's nothing wrong with it, the profit motive is there.

We've got to figure out modalities to help break down some of these silos, and maybe the only I'll be able to do is to be a convener and maybe help negotiate some of the transitions that have to take place. But Big Data takes on more than promise, because of the incredible advances in computing capabilities. Just in the last few years, of course, when we talk about the patients' data, we also have to take into account that which we haven't solved yet completely, which I think is in our reach—the privacy concerns.

And also, who owns the data? Does the patient own the data? I'm working with the Department of Energy and our national laboratories—probably the best kept and one of the most vital assets that United States of America possesses—and I met with Secretary Ernie Moniz, a brilliant scientist in his own right. He heads the Department of Energy national labs and we've initiated a project called National Strategic Computing Initiative with the goal of making supercomputers capable of a billion billion calculations per second. Our scientists in the labs think it's within reach.

They're working on a project with enormous focus, but the promise, if that occurs, is equally enormous. If we can get data in one place, the bottom line is that we need all hands on deck. Big Data captures the big picture. We can use that data to understand a person's cancer—uncover similarities and responses across large patient groups to help design the best course of therapy. But we have to break down those silos and share the data.

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Conversation with The Cancer Letter

Sigal: FDA Should Consolidate Oncology Portfolio

(Continued from page 1)

Oncology insiders are waiting to understand the meaning of the word "virtual" in the designation of the Center of Excellence at FDA. Indeed, how is a virtual center distinguishable from a brick-and-mortar establishment?

Is the proposal a signal of structural change—with far-reaching consequences—at FDA, or does "virtual" stand for a stopgap measure for dealing with ongoing debate over whether products should be regulated according to disease-oriented pathways?

Here is the exact language the White House has used:

"The FDA will develop a virtual Oncology Center of Excellence to leverage the combined skills of regulatory scientists and reviewers with expertise in drugs, biologics, and devices. This center will expedite the development of novel combination products and support an integrated approach in:

• "Evaluating products for the prevention, screening, diagnosis, and treatment of cancer;

• "Supporting the continued development of companion diagnostic tests, and the use of combinations of drugs, biologics and devices to treat cancer; and

• "Developing and promoting the use of methods created through the science of precision medicine."

Research advocates say that more than $75 million will be needed to reform the agency through the Centers of Excellence—a necessary step toward creating more efficient regulatory pathways. (The Cancer Letter, Feb. 5.)

"The Centers will improve coordination within and between FDA medical product centers and break down decades' old silos within FDA and make for a more efficient agency," said Ellen Sigal, chair and founder of Friends of Cancer Research. "This coordination will allow the agency to expedite the development of novel combination products, as well as support an integrated approach in product evaluation, support continued development of combination products, and develop and promote precision medicine methods.

"Most importantly, the proposal enhances FDA's ability to execute their vital role in translating scientific discovery into new therapies for patients."

Sigal and Friends of Cancer Research play a central and ongoing role in the development of the 21st Century Cures Act, an initiative passed by the House aimed at modernizing clinical trials and expediting

drug development.

Cellular and immunologic therapies, devices and biomarker tests are currently regulated in separate areas within FDA. This existing structure needs reform, Sigal said, and these "isolated portions" need to be brought under one umbrella for the benefit of patients.

"The regulatory structure may be adequate, yes. Yet, as those within FDA with a breadth of experience have noted, science and treatment options today have progressed far beyond this type of agency structure," Sigal said to The Cancer Letter. "Patients deserve an agency that regulates these products similarly to how they are used in medical practice. Previous efforts to develop a more disease-oriented approach to product regulation have demonstrated the positive effect of this type of organizational structure."

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

Matthew Ong: *What does the moonshot propose for FDA?*

Ellen Sigal: The moonshot creates a framework that builds upon the incredible oncology research taking place all across the country. By finding ways to streamline the FDA it creates a more collaborative ecosystem across all sectors to expedite scientific discovery.

Specifically, it calls on Congress to update FDA's structure to better reflect 21st century science by creating Centers of Excellence within FDA. The Centers will improve coordination within and between FDA medical product centers and break down decades-old silos within FDA and make for a more efficient agency. This coordination will allow the agency to expedite the development of novel combination products, as well as support an integrated approach in product evaluation, support continued development of combination products, and develop and promote precision medicine methods.

Most importantly, the proposal enhances FDA's ability to execute their vital role in translating scientific discovery into new therapies for patients.

MO: *What does the funding situation look like for the agency? How would the moonshot change funding for FDA?*

ES: Funding is a perennial challenge at the FDA. This is an agency that over time has been given more and more responsibilities by Congress. The administration's moonshot increases FDA funding by $75 million, a crucial funding increase needed to implement the types of programs proposed here. The White House has said this is part of an initial investment representing a down payment on the National Cancer Moonshot.

This funding, along with a significant increase for programs at the NIH, is meant to improve early cancer detection, take advantage of the cutting edge science of immunotherapies, increased use of genomic analysis, enhance data sharing, and establish the Oncology Center of Excellence at the FDA.

For the FDA and other agencies to achieve these types of goals, more funding than $75 million is necessary. Over the coming months, the administration has said it will be working with Congress to launch the next phase of investments, providing the resources needed to double our rate of progress in this historic fight.

MO: *Is the oncology regulatory system we have now adequate? Is it consistent with the state of science today?*

ES: The regulatory structure may be adequate, yes. Yet, as those within FDA with a breadth of experience have noted, science and treatment options today have progressed far beyond this type of agency structure. Today's techniques for cancer treatment and care are multi-modal. It makes sense for regulation of the products to use a similar approach to ensure that decisions are made in context, with consistency and involve the diverse relevant expertise across the FDA.

We need an agency that can collaborate more effectively across an entire disease so that when groundbreaking drugs are being developed, the FDA can make sure they get to patients in the safest and fastest way possible.

MO: *Can you think of a rationale for keeping all these things separate: cellular therapies, immunologic therapies, oncologic devices, biomarker tests?*

ES: The current structure has evolved over time as new authorities have been given to FDA. Advances in science and technology mean that many of these products are now being developed concurrently.

In oncology, there are more frequent instances of developing products that may involve multiple centers at FDA. For example, a drug that requires a companion diagnostic to identify patients who are most likely to benefit; or a cell-based vaccine combined with a drug.

For patients, they can't be sure they are getting the correct targeted therapy without an effective biomarker test. Having these products regulated within isolated portions of the FDA leads to incongruent timelines that may result in development delays.

This type of integration not only makes sense for oncology, but for other divisions within FDA. Breaking down these structures so that the FDA can address cancer

as a disease will show how best to streamline how the agency handles evaluation of drugs, devices, and tests across other diseases as well.

MO: *So why is the FDA Oncology Center of Excellence necessary? What can it accomplish that the existing system cannot?*

ES: This is necessary because patients deserve an agency that regulates these products similarly to how they are used in medical practice. Previous efforts to develop a more disease-oriented approach to product regulation have demonstrated the positive effect of this type of organizational structure.

In 2004, several therapeutic biologic products were relocated into the current organization for oncology drugs at FDA. This was an important change that has helped usher in a new era of anti-cancer products that in some instances are now having a profound impact on previously untreatable diseases. But this was just a first step to build on.

By forming teams of FDA staff with cutting-edge expertise in the treatment and prevention of specific disease areas, the agency can improve coordination within and between FDA medical product centers. This approach will break down decades' old silos within the agency.

It is this brand of innovative thinking that will help build a healthier America and maintain U.S. leadership in drug and device development.

Slamming the Door
Part III: 18,000 Bosses

(Continued from page 1)

On the other hand, it was possible that he graded fairly.

Soon after he was named president, at a cocktail reception in Boston, an acquaintance asked him what it was like to run MD Anderson.

"It's like this: I say, 'Look to the left,' and 18,000 people look to the left. I say 'Look to the right,' and 18,000 people look to the right."

Around the same time, in October 2011, in a talk before the Board of Visitors, DePinho mentioned those 18,000 people in a strikingly different way.

He said his 88-year-old mother was proud she was that he would be the boss of 18,000 people.

"Well, I told her, not exactly—I will have 18,000 bosses," he said. "My job will be to work for them, helping them realize their fullest potential and achieve great good for humanity. She understood completely as she and my father had instilled their children with certain core values—respect, integrity, altruism, and hard work."

***

Lynda Chin quickly emerged as a key player in his administration.

DePinho first mentions her is an email to John Thornburgh, an official with the headhunting firm that was running the search.

"On the personal level, it would be helpful to get visibility on the top private school and housing," DePinho wrote on April 7, 2011, a month before the job was offered to him. "Finally, we have Lynda's professional career. I believe it would be most productive that she be approached as an independent entity. She needs to understand the potential scientific/programmatic opportunities for her at MDA. Given her record of achievement and national leadership, she may very well be the most accomplished scientist at MDA. Thus, it is important that whatever program she leads/shapes that it not be viewed as one derived from her personal relationship with the boss."

The UT System ultimately set up an unwieldy system for managing Chin's potential conflicts. She reported to the MD Anderson provost, while the provost reported to her husband. Poor Raymond DuBois got the task of saying no to Chin's demands for a massively expensive construction of her office suite and her plans for travel.

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Almost immediately after DePinho and Chin arrived in Houston, MD Anderson facilities staff started to prepare to construct the offices of the Institute for Applied Cancer Sciences.

Usually, office space at MD Anderson is strictly regimented and the furniture tends to be heavy-duty. (An ergonomic Herman Miller Aeron office chair was considered a trapping of luxury.) IACS would be different. As a place where industry would meet academia, the offices were intended to make pharmaceutical industry executives feel at home.

Construction was so expensive that variances from the UT System's vice chancellor for health affairs, Kenneth Shine, had to be obtained.

I started hearing stories about translucent walls and modern classics. I heard something about a fabulously expensive red leather sofa that was purchased for Chin's office.

That was intriguing, of course, but it was hardly an appropriate entry point to a story. It would look petty to start coverage by focusing on the sofas.

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The MD Anderson moonshot—which would later come to be known as the Moon Shots Program—seemed to be the ray of hope DePinho planned to aim at physicians and scientists at the institution.

Sure, they would have to work harder, but at least they would know that, thanks to their efforts, cancer's butt would be kicked. Surely, the good people of Texas would see greater promise in final eradication of cancer, and, surely, the docs at MD Anderson would be selfless enough to redouble their efforts.

In reality, physicians at MD Anderson are a busy bunch. A few years earlier, when MD Anderson was in financial trouble, then-President John Mendelsohn increased the faculty's clinical revenues quotas. Now, thanks to the DePinho determination to boldly go, and explore, and all that, the quotas would rise again.

Alas, from where they sit, clinicians don't see the proximity of the cure. They see a few advances, even some great advances, but mostly they see a lot of suffering and too much death.

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DePinho's role in AVEO Pharmaceuticals Inc., his drug company, wasn't hidden. On his desk, he kept a tivozanib pill encased in clear acrylic.

It was a paperweight of sorts, which he showed to visiting dignitaries as an illustration of his orientation toward producing drugs patients could use right away. Indeed, patients in Eastern Europe were using these drugs in a clinical trial. On weekends, he was often seen sporting an AVEO windbreaker.

These displays of commercial tchotchkes reminded Houstonians that DePinho's predecessor Mendelsohn was never seen wearing ImClone orange, even though his connection with that company was even tighter. Mendelsohn was the inventor of Erbitux; DePinho wasn't the inventor of tivozanib.

Perhaps this different attitude toward conflicts of interest could be chalked up to generational differences. Perhaps old rules no longer applied. Perhaps there is an underestimated virtue in conflicts. Perhaps efficiently developing drugs should trump conflict-of-interest safeguards that shield patients from research risks.

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In March 2012, a couple of months before I started covering the CPRIT and MD Anderson story, I got a call from an old acquaintance, Leonard Zwelling.

Zwelling called more or less out of the blue, to tell me that he liked How We Do Harm, a book I co-wrote with Otis Brawley, the chief medical officer of the American Cancer Society. Our book had just come out.

A decade earlier, when our paths first crossed, Zwelling was an MD Anderson company man all the way.

His job was to defend MD Anderson and Mendelsohn in the ImClone crises. Mendelsohn served on the boards of directors of both companies. As we were exchanging pleasantries, I remembered that Zwelling would have unparalleled perspective on conflicts of interest

In his old job as vice president for research administration, Zwelling had been a chief advocate for Mendelsohn—and later became an architect of the MD Anderson policy on conflicts of interest.

Cautiously, I asked Zwelling what he thought of the new president.

Cautiously, he said that he was concerned.

Cautiously still, I asked what he was concerned about.

Conflicts of interest, he said. I had to start putting cards on the table.

"The shit you said about ImClone about ten years ago was pretty audacious," I said.

I was referring to the comment Zwelling made to The Washington Post more than a decade earlier. He said that some colon cancer patients on the MD Anderson study deliberately sought out Erbitux and viewed Mendelsohn's three roles—as the drug's inventor, an ImClone board member, and president of the cancer center conducting the trial—as a positive.

"When they find out their doctor is the person that invented something, they think that's just sliced bread," Zwelling said to the Post. "They say, 'I've come to the right place. This is the best I could hope for.'"

His statement was likely true, but irrelevant.

Yes, some patients don't worry about conflicts of interest, but all patients need to be informed about conflicts in a systematic manner. There has to be disclosure, and it has to be uniform.

Yet, it was probably a good thing that Zwelling didn't quit. In response to the ImClone debacle, MD Anderson set up a strict policy on managing institutional conflicts of interest.

To his credit, Mendelsohn had been thinking about

these issues. Mendelsohn was a clinician, formerly chief of hematology and oncology at Memorial Sloan-Kettering Cancer Center.

Even before the Post story, he didn't directly treat the patients in the Erbitux trials, and the institution continued to enroll patients in studies of other colon cancer drugs. When an MD Anderson investigator, James Abbruzzese, declined to test Erbitux in pancreatic cancer, Mendelsohn didn't try to convince him to rethink his decision.

When Post reporter Justin Gillis questioned him in 2002, Mendelsohn acknowledged that his roles as MD Anderson president and a board member at ImClone could present ethical problems.

Also he noted that MD Anderson strengthened its policies in 2001, requiring that patients be informed uniformly about conflicts, and prohibiting doctors who may have a financial stake in an experimental therapy from direct involvement in clinical care of a patient who is getting that therapy.

These actions were triggered by the death of Jesse Gelsinger, an 18-year-old patient with a genetic disorder who died at the University of Pennsylvania in 1999, after volunteering to test an experimental treatment for ornithine transcarbamylase deficiency.

"I'm not sure it's necessary even today," Mendelsohn said to Gillis in 2002. "But I think you move with the times. I don't want to take any chances that a patient will feel they've been deceived at MD Anderson."

After the Post's story, and acting on request from Mendelsohn, MD Anderson further tightened its conflict-of-interest rules. Zwelling was one of the key players in that rewrite.

Now, a decade later, DePinho and Chin were keeping their advisory and fiduciary roles at some of their companies.

The COI policy Zwelling helped craft states that "no faculty member, trainee, or institutional decision maker may serve as either a member of a board of directors, executive, or as an officer of any of the following: (1) a business, (2) other legal entity, or (3) a competitor of MD Anderson."

Did that mean that DePinho and Chin were operating in violation of the MD Anderson COI policy? The answer had to be yes.

Of course, the UT System officials knew about DePinho and Chin's industry involvements. The conflicts and plans for their management were noted in Shine's offer letters to the couple.

Yet, no formal waiver was issued. Did that mean that, from day one, DePinho and Chin were employed in violation of the COI policy?

I asked Zwelling whether he thought I was hallucinating. He assured me that I wasn't. He couldn't see how anything less than a waiver would suffice.

The waiver would indeed be issued, but not until late 2012, which meant that DePinho and Chin operated in violation of MD Anderson's COI policies for more than a year.

I knew that eventually I would have to jump in and write something about MD Anderson, but I wanted my first story to be more than a recap of the Houston Chronicle's excellent coverage. I was waiting for something with oomph.

I recall his sign-off that afternoon:

"Gotta run," Zwelling said. "We are going to the moon."

***

In May 2012, I learned about an effort to obtain at least $18 million a year in CPRIT funds to fund Chin's Institute of Applied Cancer Science.

Was CPRIT funding promised to DePinho and Chin at the time they were being recruited to relocate to Texas?

Earlier this year, I asked Dan Fontaine, executive chief of staff at MD Anderson, whether they were promised that CPRIT money would be used to fund IACS.

"Actually, in terms of the conversation between the University of Texas System and Dr. DePinho and Dr. Chin, the only thing that I'm aware of on the CPRIT front was the encouragement for the application for recruitment dollars, I believe, for Dr. Chin, which I believe was successfully done. And I'm going on memory here," Fontaine said. Indeed, Chin received a recruitment grant from CPRIT.

"On the other side, at [IACS], I don't think there was ever a promise of CPRIT funding for that. To the contrary, I think as the institution made its commitment to the funding of the [IACS], the UT System impressed upon both us, as well as with other conversations I think with Dr. [Guilio] Draetta [director of IACS], that there was certainly a desire on UT System's part for [IACS] to look for support and external funding.

"And at that point in time I'm sure CPRIT was pointed to as a source, because CPRIT was not only funding research—but also, as reflected back in the stuff that you looked at at that time—was also putting forward grants to attract companies to Texas. And to

transfer other types of things that would help build the type of infrastructure, an ecosystem if you would, for the biomedical development that CPRIT was trying to accomplish for cancer.

"So I don't think there was ever a promise of CPRIT funding, but to the contrary, I think the UT System officials, both us at MD Anderson as well as people at CPRIT, to look and make applications if the opportunity arose to support IACS."

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At CPRIT, the maneuvers to undermine Al Gilman began subtly, invisibly.

In 2011, CPRIT altered its rules to allow biotechnology incubators to be funded with review by a panel that would focus exclusively on the commercialization potential of the project.

In those cases, a review of the science underlying the project wouldn't be required.

Indeed, review of all of the small incubator projects would be cumbersome, and the incubators needed to move quickly and flexibly with their decisions. The scientific quality of their operations could be judged after a few years of experience.

Gilman did not object to this, although this move would become a crucial element in all of the bad things that nearly led to CPRIT's demise.

The fact that the move was proposed by Charles Tate, a financier with close ties to the governor and lieutenant governor, didn't excessively alarm Gilman either.

Provenance notwithstanding, the idea made sense. Incubators are usually places where scientists can do research in a non-academic environment to explore the commercial potential of an idea, hopefully getting it to the point where investors can be brought in.

This separation is good. It safeguards commercial research from being confused with campus research. This separation also makes it possible to separate university employees from employees of private companies.

Gilman was no opponent of commercialization. Though a creature of campus, he serves on two corporate boards. He is a member of the board of directors of Eli Lilly & Co. and Regeneron Pharmaceuticals Inc.

Gilman saw no cause for concern. At the time, he didn't even know he had adversaries.

When the regents announced that they had selected DePinho to lead MD Anderson, Gilman remained neutral about the choice. He knew a bit about DePinho and next to nothing about Chin.

When MD Anderson applied for a $5 million grant to enable the recruitment of Chin as a CPRIT scholar, several members of the scientific council noted that she is abrasive and has even higher self-esteem than her husband. But her science was good enough, and that was all that mattered. The people of Texas were well served by having a decent scientist like her relocate to the state.

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In December 2011, Bill Gimson, CPRIT's executive director, asked Gilman to meet with Chin. A three-way videoconference conference was arranged.

Chin presented what struck Gilman as a quasi-business plan, free from scientific detail, for early drug discovery research that would be conducted at her institute. The institute would employ people Chin brought with her from Boston as well as former business people. The institute was a new construct.

MD Anderson would keep commercialization on-campus at least for some extended period. It was unclear when they would seek to spin off new companies or license their discoveries to established companies.

Clearly, that would create conflicts that would be hard to manage. For example, would people working for the commercial entity be paid on the same pay scale as faculty members? Would they be faculty members? Should they be faculty members? How would faculty members who work for a company carry out their obligations as teachers? Would the students and postdocs who work for these faculty members be working in the company's laboratory? Would company work be done on state-owned university campus space? Would that be appropriate?

As Gilman saw it, much of the work done at a company is turning-the-crank sort of stuff. It needs to be done, but it doesn't teach postdocs how to run research programs.

There are also issues of secrecy and locked doors. The whole atmosphere of a university is supposed to be open. People wander around and share ideas, discoveries and knowledge. But a company has a financial imperative and fiduciary responsibility to its investors to keep secrets secret and protect intellectual property.

By folding a pharma industry structure into an academic environment, you invite academics to wonder why they are doing all the traditional academic work while their colleagues sit behind closed doors, trying

to get rich.

You magnify the potential for things going wrong, Gilman believed.

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During the videoconference, Gilman told Chin that the work she described amounted to a large-scale research project that would need to be submitted as a multi-investigator collaborative proposal.

Though she referred to the project as an incubator, an incubator it was not. Chin was requesting money for her institute. She would then use the funds as she saw fit.

Chin sounded like the sort of person who doesn't take no for an answer. She was obviously annoyed by Gilman's suggestion that she submit a grant proposal like everyone else.

Chin argued that Gilman and his scientists didn't have the expertise to review commercialization efforts and that the CPRIT budget limits were too stringent.

Gilman first noted several of CPRIT's reviewers with commercial expertise and then replied that CPRIT had no budget limits for multi-investigator proposals.

"Yes there are," Chin replied.

"No there aren't," replied Gilman, who, being the engineer of CPRIT, designed its rules for funding science.

During that video conference, while talking with Chin, Gilman sent Gimson an email, saying the Chin obviously didn't want to apply for a grant. She just wanted the money.

Indeed, documents show that Chin's appetite for money was gargantuan: she wanted $75 million over three years from CPRIT, to be matched by MD Anderson. Though CPRIT had no limit on such grants, $25 million a year would have been extraordinary indeed.

More importantly, handing out money without scientific justification and with no strings attached would have constituted a betrayal of public trust, Gilman believed. It would have been grossly unfair to all other Texas cancer scientists who were writing grant applications.

The conversation was unpleasant enough, but Gilman didn't reflect on it much. He simply returned to work.

Next week: **Part IV – A Nobel Laureate n the Crosshairs**. Click here to read the full series of Slamming the Door.

In Brief

Miami Cancer Institute to Join MSK Cancer Alliance

THE MIAMI CANCER INSTITUTE at Baptist Health South Florida joined the **Memorial Sloan Kettering Cancer Alliance**, making it the third health care system to enlist in the national collaboration.

"The enhanced treatments and clinical care we can now offer—including standards that align with MSK for surgical procedures, chemotherapy, and radiation therapy—will have a near-immediate impact on our patients," said Michael Zinner, founding CEO and executive medical director of Miami Cancer Institute.

"In the near future, Miami Cancer Institute will provide access to cutting-edge research, including MSK's world-renowned clinical trials and protocols and breakthroughs in promising new fields, such as molecular oncology."

Over the next few months, MSK will collaboratively guide Miami Cancer Institute toward standardizing patient care and clinical cancer research programs in line with MSK Cancer Alliance. Once this first phase is complete, Miami Cancer Institute is expected to become an official member of the MSK Cancer Alliance over the next year.

Alliance members will share educational resources, including opportunities for its physicians to visit MSK's Manhattan facilities to observe new techniques, and it will begin the process of putting into place the infrastructure necessary to measure outcomes data.

Some Miami Cancer Institute physicians will also have the opportunity to meet with and discuss their more complex cancer cases with MSK physicians, who have experience in treating different forms of cancers and related blood disorders, including cancers that are simply not often seen in a community setting.

Central to the MSK Cancer Alliance is expanding clinical trials and being able to provide Miami Cancer Institute patients with the opportunity to participate in trials not previously available.

SURESH RAMALINGAM was named deputy director of the **Winship Cancer Institute of Emory University**. He will also serve as assistant dean for cancer research at the Emory School of Medicine.

Ramalingam will lead the integration of the

research, clinical, and educational components within Winship. This position was previously held by Fadlo Khuri, who assumed the presidency of American University of Beirut in August 2015.

A professor in Emory's Department of Hematology and Medical Oncology, he now serves as director of medical oncology and the Lung Cancer Program. He currently co-leads Winship's Discovery and Developmental Therapeutics Program.

"We are very fortunate to have Dr. Ramalingam serve in these pivotal leadership roles at Winship and the School of Medicine," said Christian Larsen, dean of the Emory University School of Medicine and CEO of The Emory Clinic. "His range [of] experiences and breadth of understanding of the cancer research landscape are exceptional—spanning target and drug discovery, exciting new developments in immunotherapy and value-oriented health services research."

Ramalingam chairs the Thoracic Malignancies Committee and serves as deputy chair for the Therapeutics Program within ECOG ACRIN.

His research focuses on agents that inhibit pathways for specific lung cancer mutations. He is also investigating ways to individualize therapies in patients with small cell and non-small cell lung cancer.

Ramalingam has authored over 200 scientific publications and is the section editor for chest diseases for the journal Cancer. He is on the editorial boards of the Journal of Clinical Oncology, Annals of Oncology, and Clinical Lung Cancer.

DAVID MCCONKEY was appointed director of the **Johns Hopkins Greenberg Bladder Cancer Institute**, which includes members of the Sidney Kimmel Comprehensive Cancer Center, the James Buchanan Brady Urological Institute, and the school of medicine's departments of Radiation Oncology and Molecular Radiation Sciences, Surgery, and Pathology.

The institute was established in 2014 with a $15 million gift from Baltimore-area commercial real estate developer Erwin L. Greenberg and his wife, Stephanie Cooper Greenberg, and a $30 million investment from The Johns Hopkins University.

He is also chair for translational medicine for the Genitourinary Cancers Committee of SWOG, and has been involved in setting agendas for the Bladder Cancer Advocacy Network's clinical initiatives.

McConkey comes to Johns Hopkins after serving as director of urological research at MD Anderson Cancer Center. He played a leadership role in MD Anderson's multidisciplinary bladder cancer research program since its inception in 1998 and served as co-principal investigator of the MD Anderson Specialized Program of Research Excellence in Bladder Cancer, which is now in its third continuous cycle of NCI funding.

McConkey joined MD Anderson in 1993 as an assistant professor in the Department of Cancer Biology and assistant professor at the University of Texas Graduate School of Biomedical Sciences. He was promoted to associate professor in the Department of Cancer Biology in 1999 and professor in the departments of Cancer Biology and Urology in 2007. McConkey was named director of urological research in 2007.

THE UNIVERSITY OF MIAMI Sylvester Comprehensive Cancer Center created two endowed chairs in head and neck oncology. These are the first two chairs of the "100 New Talents for 100 Years" initiative announced by President Julio Frenk at his inauguration address.

The W. Jarrard Goodwin Jr., M.D., Endowed Chair in Head and Neck Oncology Surgery was established with a gift from the Harcourt M. and Virginia W. Sylvester Foundation, and will be held by **Donald Weed**, co-director of the Division of Head and Neck Surgery at Sylvester and professor of otolaryngology at the University of Miami Miller School of Medicine.

The Virginia M. Horner Endowed Chair in Head and Neck Oncology Research was established with a gift from Virginia Horner, and will be held by **Francisco Civantos**, co-director of the Division of Head and Neck Surgery/Otolaryngology, and professor of otolaryngology - head and neck surgery at the school of medicine.

The university hopes to fund 100 new endowed faculty chairs before 2025, with a mix of senior, junior and visiting professorships.

"Jerry Goodwin has had a tremendous influence on my academic career, and it is deeply meaningful to me to now be associated with his name and his wonderful legacy here at Sylvester," said Weed.

"The support that comes with an endowed chair will be instrumental in my being able to conduct research as a clinician and investigator by helping to assure that I will have the time to fully devote myself to these efforts. As our many efforts in research, teaching and even clinical care are becoming increasingly under-funded, the long-term support of an endowed chair is

critically necessary for individuals and for departments to be able to advance their clinical, educational and academic missions."

PAT KEEL was appointed chief financial officer of **St. Jude Children's Research Hospital**.

Keel was most recently with University Health System in Shreveport, Louisiana, where she served as chief financial officer and senior vice president. In addition, she held leadership roles with Good Shepherd Health System in Longview, Texas and CHRISTUS Schumpert Health System in Shreveport.

She received a William G. Follmer Bronze award from the Healthcare Financial Management Association. In December 2015, Keel was named to Becker's Hospital Review 130 women hospital and health system leaders to know.

PAUL VANVELDHUISEN was named chief operating officer of **The Emmes Corporation**. VanVeldhuisen will continue to serve as principal investigator for government and privately funded research projects.

VanVeldhuisen joined the company in 1993 and was promoted to vice president in 2006. He is responsible for the scientific aspects of various research studies, including study design and analysis, and he oversees day-to-day operations of clinical trial support. VanVeldhuisen has contributed to research in important public health areas, including ophthalmology, drug abuse, organ transplantation and infectious disease. He also received the company's Public Health Impact Award in 2013 for his team's research on the safety of cesarean sections.

THE AMERICAN UROLOGICAL ASSOCIATION, the **Urology Care Foundation** and **Chesapeake Urology Associates** formed a $1 million partnership, establishing the Community-Based Research to Advance Prostate Cancer Care program.

The program will involve data from community urology practices; helping urologists develop research partnerships and collaborations; scholarships for urologists and academic physician-scientists and researchers; services such as study design, data collection, integration, analysis, and reporting; and consultation services to increase research funding and publication.

THE BONNIE J. ADDARIO Lung Cancer Foundation launched the second phase of its Clinical Trial Innovation Prize crowdsourcing challenge in honor of World Cancer Day. The goal of the challenge is to produce breakthroughs that will double the patient accrual rate of clinical trials evaluating interventions in the diagnosis and treatment of all cancers.

"The problem of patient accrual to clinical trials is multi-factorial, and may be attributed to several factors such as a lack of awareness among some patients and physicians, procedural inefficiencies, stigmas and misconceptions, geographic, language or socio-economic barriers, which contribute towards multiple clinical trials being prematurely halted, wasting precious research dollars and delaying cancer patients' access to cutting edge diagnostics and therapies," said Guneet Walia, the foundation's director of research and medical affairs. "Through this crowdsourcing challenge, we hope to, one, raise awareness around this problem; and, two, identify some unique solutions coming from innovators from across the world who are willing to look at the problem with a fresh pair of eyes and unique insight so that we can drive patient accrual to oncology clinical trials."

The first phase of the prize was launched on World Cancer Day, Feb. 4, in 2015, and focused on innovators sharing creative and novel ideas on how to double the accrual rate of cancer clinical trials. The second phase, the Implementation phase, asks competitors to provide proof and data that their ideas have indeed resulted in an increase in trial participation.

ESPN's 2015 Jimmy V Week for Cancer Research raised $3.2 million for **The V Foundation for Cancer Research**—a million more than the $2.2 million raised in 2014. In nine years, Jimmy V Week has raised $13.7 million for cancer research.

Jimmy V Week ran from Dec. 2-8, 2015 and introduced the awareness campaign Your Fight is Our Fight.

The campaign included the annual Jimmy V Women's and Men's Basketball Classics Presented by Corona, featuring three-time defending national champion UConn hosting Notre Dame on Dec. 5, as well as four top college basketball programs in the men's event on Dec. 8: West Virginia vs. Virginia and Maryland vs. UConn.

More than $1.2 million was presented at the Jimmy V Men's Basketball Classic from Corona, Hooters, the Champions League and New York Road Runners with Team V, which helped push the total to over $3 million.

Drugs and Targets

FDA Grants Orphan Drug Designation to Tazemetostat

FDA granted orphan drug status to tazemetostat, an EZH2 inhibitor developed by Epizyme Inc., for malignant rhabdoid tumors.

In December 2015, Epizyme initiated a phase II study in adults and a phase I study in children with genetically defined tumors, including MRTs. Tazemetostat is also being investigated in an ongoing five-arm phase II study in patients with non-Hodgkin's lymphoma.

Orphan drug designation provides the sponsor of the drug with eligibility for various development incentives, including tax credits for qualified clinical testing and marketing exclusivity for a period of seven years.

MRT is a tumor defined by loss of INI1 protein as measured by immunohistochemistry. Other rhabdoid tumors, such as MRT of ovary, are characterized by loss of the protein SMARCA4 and have shown sensitivity to tazemetostat in preclinical models and the phase I study. The orphan drug designation applies to both INI1-negative MRT as well as SMARCA4-negative MRT of ovary.

EZH2 is a histone methyltransferase that is increasingly understood to play a potentially oncogenic role in a number of cancers. These include non-Hodgkin lymphoma, INI1-negative cancers such as malignant rhabdoid tumors and epithelioid sarcomas, certain SMARCA4-negative solid tumors, synovial sarcoma, and a range of other solid tumors, according to Epizyme.

In some human cancers, aberrant EZH2 enzyme activity results in dysregulation of genes that control cell proliferation resulting in the rapid and unconstrained growth of tumor cells. Tazemetostat is the WHO International Non-Proprietary Name for compound EPZ-6438.

PDS Biotechnology signed an Cooperative Research and Development Agreement with NCI to co-develop several immunotherapies through phase II clinical trials to be initiated in 2016 and 2017, utilizing combinations of PDS's Versamune with NCI- and PDS-sourced tumor-related proteins or their antigens in prostate, breast, and HPV-related cancers.

The PDS-NCI CRADA collaboration is led by Jay Berzofsky, chief of the NCI Center for Cancer Research Vaccine Branch; Lauren Wood, head branch's Clinical Trials Team; and Masaki Terabe, deputy section chief of the branch.

"The Versamune platform, based on preclinical and phase I human clinical studies, has demonstrated the potential to overcome the most critical obstacles facing cancer vaccine technologies. Versamune enables the design of simple subcutaneous immunotherapies that efficiently deliver tumor antigens to the patient's own immune system, while simultaneously stimulating the generation of potent tumor-killing T-cells that can overcome the tumor's immuno-suppressive environment. We are very pleased to have the opportunity to collaborate with Drs. Berzofsky, Wood, and Terabe, to extend the clinical progress that has been achieved to date with our Versamune platform and the immunotherapy field in general," said Frank Bedu-Addo, PDS president and CEO.

FDA granted orphan drug designation to antifungal drug candidate CD101 IV, developed by Cidara Therapeutics Inc., for the treatment of candidemia and invasive candidiasis.

The seven-year period of marketing exclusivity provided through orphan designation combined with an additional five years of marketing exclusivity provided from the previously announced QIDP designation gives CD101 IV for a total of 12 years of potential marketing exclusivity to be granted at the time of FDA approval. CD101 has also received an FDA Fast Track Designation.

"This designation underscores the need for new drugs to treat severe fungal infections and is another in a series of milestones that demonstrate the promise of our novel, long-acting echinocandin, CD101 IV," said Jeff Stein, president and CEO of Cidara. "Our phase I data demonstrating the safety and tolerability of up to three doses of high exposure, once-weekly CD101 IV enables us to initiate our phase II study in candidemia early this year. We believe CD101 IV has the potential to become a best-in-class echinocandin antifungal."

In January, Cidara reported data from its phase I multiple ascending dose clinical trial of CD101 IV, which demonstrated safety and tolerability across a broad range of doses. The company plans to initiate a phase II candidemia trial in the first half of this year.