THE CANCER LETTER

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News Analysis

DePinho Bets MD Anderson Credibility On His Cancer "Moon Shot" Program

By Paul Goldberg

Later this month, at MD Anderson Cancer Center, Ronald DePinho will announce the details of something he unabashedly calls the "moon shot," a plan for dramatic reduction of mortality for at least five cancers.

The date of the announcement—Sept. 21—wasn't arrived at by chance.

It comes five decades and nine days after President John F. Kennedy's "we choose to go to the moon" speech, delivered at Rice University, also in Houston.

MD Anderson President DePinho is by no means the first cancer politician-scientist to risk angering the gods and nature by promising a giant leap toward the cure. Vows of this sort were a prominent part of political buildup that produced the National Cancer Act of 1971 and have resurfaced regularly since.

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A Year in Houston

DePinho Reflects on Plans, Conflicts, Controversies—and Lessons Learned

The Cancer Letter invited MD Anderson President Ronald DePinho to reflect on his first year as head of the cancer center.

The interview offered new perspective on his approach to managing conflicts stemming from relationships with industry, the role his scientist-wife Lynda Chin plays at MD Anderson, and his plans for what he calls "the Moon Shot Program."

DePinho also provided his perspective on the controversies that arose during his first year at MD Anderson, particularly stemming from Chin's biotechnology "incubator," which received $20 million in Texas state funds, but was ultimately withdrawn, to be resubmitted at a later date.

The interview was conducted by Paul Goldberg, editor and publisher of The Cancer Letter.

PG: In your job interviews, originally with the UT System chancellor and the regents, you were asked, I'm sure, to describe your vision for MD Anderson. In a nutshell, what were the plans you described for them?

RD: The interview process was a very essential and lengthy one, during which I was asked to describe my vision for MD Anderson and for cancer care in the future, which, I'm sure, was asked of all the candidates.

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The Cost of Change: Revenue Targets Rise for Clinicians

(Continued from page 1)

The most recent official to pledge to defeat cancer was former NCI director, former FDA commissioner—and former MD Anderson official—Andrew von Eschenbach. DePinho's moon shot is all the more ambitious, because it emanates from a cancer center, not from NCI or the White House. No blueprints have leaked out, and it's not at all clear how MD Anderson would play the role of mission control.

DePinho has been making bold promises since coming to Houston a year ago, but has moderated his stance in recent months, inserting some caveats and refraining from using the word "cure." Yet, even qualified, the words "moon shot" are loaded.

The analogy implies that advances in basic science have made cancer into a cluster of engineering problems—akin to the problems Kennedy had pledged to solve to reach the moon.

In an interview with The Cancer Letter, DePinho said that new understanding of cancer makes the moon shot approach feasible.

"We have reached a point where there is a confluence of technological advances and significant conceptual breakthroughs and clinical proof of concept, such as harnessing the power of the immune system, affecting cell cycle, altering apoptotic responses, and a variety of other hallmarks for cancer where we have drugs that target those hallmarks result in clinical responses, some of which are quite dramatic, that puts us in a position to say that if we organize ourselves in a comprehensive way, in an integrated way, from prevention to early detection to prognostication to treatment and survivorship and recurrence, that we can significantly reduce mortality in this decade for certain cancers," he said.

"There are some cancers where we're showing very impressive progress, if we apply what we already know today in a way that is translated and reduced to practice to help patients—in the area of early detection, for example, or in the area of combining very potent drugs with very significant clinical responses—we will dramatically reduce mortality in those cancers."

The interview, in which DePinho reflects on his tumultuous first year at MD Anderson and explains what precisely he has in mind for the future, appears on page 1.

"Kicking Cancer's Butt"

Last November, two months after he moved to Houston from Dana-Farber Cancer Institute, DePinho seemed to have needed fewer caveats.

At a fundraising event in San Antonio, the researcher, who is also a martial arts expert, pledged on camera to "kick cancer's butt."

At the same fundraiser, he said that if the cure for cancer is not found on his watch, he would consider his tenure a failure. "And I will not fail," he pledged to a room full of people, according to a story in the San Antonio Express-News.

Alas, moon shot strategies have been known to lead entire institutions—primarily NCI—into a world of fantasy. Goals as big as the cure can become all-consuming, taking on lives of their own. The hunt for the cure isn't something that can be done in moderation; it has to click into place as the central organizing principle in the functioning of an institution.

In the business of moon shots, von Eschenbach clearly defines the worst-case scenario. The George W. Bush appointee reviewed all NCI programs based on how they would contribute to his "challenge goal" to "eliminate suffering and death due to cancer" by the year 2015.

He reorganized the institute around his favorite alliteration: discovery, development and delivery—which he referred to as "the three Ds." He reshuffled NCI resources, devoting hundreds of millions of dollars to farfetched programs in bioinformatics, biospecimens and nanotechnology. These programs have since been cut drastically or eliminated.

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As he claimed triumphs, von Eschenbach had to devote ever-increasing efforts to convincing skeptics that while we are not there yet, the goal is getting closer. On the propaganda front, he launched a weekly NCI publication to hail heroic conquests and publish his photographs.

People who knew that the real world was elsewhere—which included just about everyone in oncology—rolled their eyes, but few had the courage to object out loud (The Cancer Letter, May 19, 2006).

This doctrinaire, grinding foolishness ended as suddenly as it began: the Bush administration dispatched von Eschenbach to head FDA, where he was ordered to stop talking about his visions for 2015.

Building Basic Science at MD Anderson

There is no reason to think that DePinho is being anything but sincere in setting his sights on the moon shot.

This cannot be an expedient, opportunistic goal. Avoiding big promises would have been safer, but DePinho appears to be the sort of player who chooses the most aggressive strategy he can devise.

He seems to stand constantly poised to recount the stories of his Portuguese immigrant parents, and, particularly, his father's death from colon cancer. That landmark in DePinho's life made him turn away from less goal-directed pursuits of science and focus directly on curing cancer by following leads from lab bench to commercialization, he says.

It would be insane to doubt that DePinho wants to kick butt; he wants you to know that this thing is personal—a grudge match.

And, to be fair, DePinho, unlike urologist von Eschenbach, is a distinguished basic scientist.

When the University of Texas System regents chose DePinho over other candidates vying for the top job at MD Anderson, they in effect gave him the mandate to build basic science at the institution that has been the powerhouse of clinical research and clinical care.

Change this profound has to entail a shakeup, and the regents had to realize and welcome that as well.

MD Anderson is a massive organization that employs 19,000. The institution has a from-the-top-down structure, with politically weak divisions and a faculty senate that has little power. Size notwithstanding, it's more malleable than many other cancer centers.

To launch the moon shot, DePinho has to recruit top-tier basic scientists and find money, perhaps billions.

One obvious source of funds, as DePinho acknowledges in his Q&A with The Cancer Letter, would be the Cancer Prevention and Research Institute of Texas, a state agency that has relied on rigorous peer review to distribute $300 million a year to researches around the state.

"CPRIT certainly would have a role from the standpoint that part of the way that we're going to be funding this is through a combination of philanthropy as well as through grants from

Moon Shot Milestones

Source: MD Anderson

Nov. 11

Moon shots vision announced (watch the townhall)

Feb. 16

Meeting with about 50 faculty, leaders and content experts to discuss in detail the program vision and components and the process for selecting the cancers that will be moon shots

February—July

More than 350 people worked on teams that created strategic scientific and business plans for 11 cancers considered for initial moon shots:
- bladder cancer
- chronic lymphocytic leukemia
- colorectal cancer
- glioblastoma multiforme
- lung cancer
- myelodysplastic syndrome-acute myeloid leukemia
- melanoma
- pancreatic cancer
- prostate cancer
- renal cell carcinoma
- women's cancer (breast and ovarian)

March 27

Meeting with faculty potentially submitting moon shot proposals to clarify guiding principles, project organizational structure and supporting platforms (watch the meeting)

July 20/21

Proposals for 11 cancers presented to internal and external reviewers for scoring. See below for list of reviewers

Aug. 2

Reviewers' comments discussed with members of the Research Council

Sept. 21

National announcement

foundations as well as through a number of other federal grants," DePinho said to The Cancer Letter.

However, CPRIT funds cancer research throughout Texas, and historically UT Southwestern has beaten all other institutions in competition for these grants.

With federal money running scarce, and with foundations hampered by lackluster economy, MD Anderson's clinical revenues may be the most reliable source of money, at least for the near term.

Raising Revenue Targets

Recently, clinical departments at MD Anderson were asked to increase their revenue targets by 5 to 10 percent, causing doctors to complain privately about increasing what they say is already a grueling clinical workload to support a lofty goal that many clinicians are unable to visualize.

Supporters of the moon shot say that work on the proposals has created excitement among MD Anderson faculty, engaging 350 faculty members, who competed to propose several projects.

On Aug. 30, on an MD Anderson faculty blog, Warren Holleman, a marriage and family therapist who serves as professor of behavioral science and director of the Faculty Health & Well-Being Program, expressed concern about increasing pressures on clinicians:

"[When] I started hearing reports about a new budget that involved increasing the productivity/revenue of our clinicians, and two thoughts came immediately to mind.

"My first thought was that this call to work harder comes at a time when we have an epidemic of burnout among our physicians—and probably nurses as well. Asking them to work harder is going to have adverse effects on their already impaired health. Asking them to bear even more of the burden of keeping this big enterprise financially afloat does not seem fair, either.

"I realize that there are no easy answers to our budgetary problems, but for the sake of our clinician colleagues let's put some other options on the table. Could we increase our revenue in other ways, such as by hiring more doctors and mid-level providers? Could we reduce our expenses by addressing a psychiatric problem common to all large organizations: the Edifice Complex?

"Every time we build a new building that isn't a clinic, it means that our physicians have to work harder to pay for that building and the people who work in it. There is a limit to how much they can do, and many of the clinicians I talk to believe they have reached that limit.

"Could we reduce expenses by reducing the size of our non-clinician workforce? This is painful to think about, but it may be necessary. (Full disclosure: Even though I am a faculty member, my salary comes from the administrative side of the budget.)

"It's not that those of us on the administrative side don't work hard or don't do our best to further the mission of MD Anderson. It's just math. There may be more of us than the current number of clinicians can support.

Moon Shot Reviewers

A list of individuals tasked with reviewing the moon shot proposals

- **Jim Allison,** director, Ludwig Center for Cancer Immunotherapy, Memorial Sloan-Kettering Cancer Center. Chair of Immunology at MD Anderson starting Sept. 1
- **Michelle Barton,** professor, biochemistry and molecular biology
- **Tom Buchholz,** head, radiation oncology
- **Lynda Chin,** chair, genomic medicine
- **Riccardo Dalla-Favera,** director, Institute for Cancer Genetics, Columbia University Medical Center
- **Sharon Dent,** chair, molecular carcinogenesis
- **Giulio Draetta,** professor, genomic medicine
- **Raymond DuBois,** provost and executive vice president
- **John Frenzel,** professor and chief medical information officer
- **Marshall Hicks,** head, diagnostic imaging
- **Waun Ki Hong,** head, cancer medicine
- **Tyron Hoover**, director, biorepository regulatory support
- **Raghu Kalluri,** chair, cancer biology
- **Eugenie Kleinerman,** head, Pediatrics
- **Charles LeMaistre,** past president
- **Leon Leach,** executive vice president
- **Jack Lee,** professor, biostatistics

"My second thought when I heard about these new, higher revenue targets: 'It's déjà vu all over again.' We did this three years ago during the recession and we burned out a lot of our clinicians by asking them to see more patients, work more hours, and skip their vacations. Then, when we pulled out of the financial crisis, we threw salt on the wound by giving top executives huge bonuses—even though the clinicians were the heroes, the ones who pulled us out of the crisis.

"We pushed many of our clinicians to the limit, and there is still a lot of residual fatigue, frustration, and anger. They are professionals, highly committed to caring for their patients, but should our solution to every financial crisis be to ask them to work harder and do more?

"Especially when research has just shown that such a high percentage are at or near the limit of their physical, mental, emotional, and spiritual strength? Is it wise to place your most valuable resource at such risk? I don't pretend to know how to run a big organization, but I do believe we should pay close attention to practices and policies that adversely affect the health and well-being of our greatest resource."

Several physicians have left the institution, and several said to The Cancer Letter that they are interviewing aggressively. Speaking confidentially, directors of cancer centers across the U.S. acknowledge that they view reorganization at MD Anderson as an opportunity to recruit excellent clinicians.

Organizational and personnel changes at the cancer center have occurred rapidly and, according to insiders, are about to accelerate.

On Aug. 27, Raymond DuBois said he would step down as provost and executive vice president. His resignation becomes effective Oct. 1.

"After five years in this important executive position, he's eager to pursue new opportunities that will enable him to further advance his career and contribute to progress over cancer," DePinho wrote in an announcement to the staff. "I am grateful to him for having agreed to stay in his key role throughout my first year as president of MD Anderson, which has been immensely helpful to me.

"In this past year alone, he has helped plan our comprehensive Moon Shots Program efforts, spearheaded the recruitment of many CPRIT-supported investigators, set our graduate program on a course to achieve national prominence, established new forward-looking departments and institutes, enhanced our mentoring programs, enabled increased grant support from the NCI in a time of decreasing paylines, and bolstered the international collaborative relationships of Global Academic Programs and our sister institutions." DuBois's resignation came as no surprise to insiders.

He had been a candidate for the president's job, and it was clear that he was not asked to sign off on some important decisions, including the proposal for a biotech "incubator," which involved DePinho's wife, MD Anderson scientist Lynda Chin (The Cancer

- **Elaine Mardis,** professor of genetics, Washington University School of Medicine
- **Frank McCormick,** director, UCSF Helen Diller Family Comprehensive Cancer Center
- **Funda Meric-Bernstam,** professor, surgical oncology
- **Jeffrey Myers,** professor, head and neck surgery
- **Raphael Pollock,** head, surgery
- **David Rimm,** professor of pathology, Yale University
- **Barbara Summers,** vice president, nursing
- **Simon Tavare,** professor of cancer research (bioinformatics) and applied mathematics and theoretical physics, University of Cambridge

Letter, May 25).

While a national search is underway, Thomas Buchholz, the division head of Radiation Oncology, will serve as provost ad interim.

Effective Sept. 1, Sharon Dent, chair of Molecular Carcinogenesis, started to serve as vice provost for laboratory and basic science ad interim. Waun Ki Hong will continue to serve as vice provost for clinical research.

In his letter, which circulated to MD Anderson staff, DuBois notes the hardships placed on the institution's doctors.

"Day after day, under the most difficult circumstances and treating the most challenging patients, they continually demonstrate not only a unique level of medical skills, but also deep compassion when dealing with an extremely vulnerable patient population," he wrote. "I have enjoyed working with the Department Chairs and Division Heads, who truly are a resilient group of professionals and who have kept things humming through good times and challenging times.

"I wish Dr. DePinho and his team every success in taking MD Anderson to the next level of cancer care."

Departures are difficult to attribute to any single cause. Some are bona fide retirements, others occur because better opportunities turn up, and still others are firings. Whatever the causes, the following high-level departures occurred on DePinho's watch:

• Lynn Vogel left his job as chief information officer.

• Scott Lippman, chair of thoracic and head and neck oncology, left to become director of the UC San Diego Moores Cancer Center.

• Razelle Kurzrock, chair of the phase I program, is packing to go to UCSD.

• Gabriel Hortobagyi, chair of breast medical oncology, will be stepping down from that position.

• David Gershenson will be leaving his position as chair of gynecologic oncology.

• Geoffrey Robb is stepping down as chair of plastic surgery.

• Valen Johnson has left his position as deputy chair of biostatistics.

• Ralph Arlinghaus is leaving his job as chair of molecular pathology.

• William Klein is stepping down as chair of biochemistry and molecular biology.

On the other side of the ledger, DePinho has recruited:

• Sam Hanash, an expert in molecular diagnostics, who came to MD Anderson from Fred Hutchinson Cancer Research Center,

• James Allison, a molecular immunologist, who came to MD Anderson from Memorial Sloan-Kettering Cancer Center,

• Raghu Kalluri, a Harvard researcher who focuses on the role of cell and tissue microenvironment in the origin and progression of cancer, and

• Andy Futreal, a genomic medicine expert, who moved to MD Anderson from the Wellcome Trust Sanger Institute.

Political Fallout

Over the past 12 months, DePinho has triggered many explosions.

Some involve the role of his wife Lynda Chin, both at MD Anderson and in Texas politics.

Chin reports to Kenneth Shine, executive vice chancellor at the UT System Office of Health Affairs.

While some insiders describe Chin and DePinho as closely aligned in running MD Anderson, DePinho describes a more distant working relationship.

"Dr. Chin plays a very important role, just as all of our department chairs do," he said. "She is chair of a new department of genomic medicine… She'll sink or swim on her own scientific merit and accomplishment here."

Recently, Chin and DePinho set off a political landmine, when a biotech "incubator" which she co-directed received a $20 million single-year grant from CPRIT.

That grant—the largest in the state agency's history—was awarded based on a six-and-a-half-page proposal that was submitted without review by MD Anderson Provost DuBois (The Cancer Letter, May 25).

This controversy triggered the resignation of Alfred Gilman from the position of CPRIT's chief scientific officer. Gilman, a Nobel laureate, said that Texas politics trumped science in the handling of the grant.

A subsequent investigation by the regents didn't attribute the problems to nepotism, but found that standard procedures had been disregarded. MD Anderson has withdrawn the proposal, but intends to resubmit it. Next month, following review of a round of grants, some scientific reviewers whose participation made CPRIT into a widely respected funding organization may follow Gilman out the door.

Other controversies were triggered by DePinho's role as a shareholder and fiduciary at several companies, at least one of which, AVEO Pharmaceuticals, sponsors a clinical trial in which MD Anderson wants to participate

(The Cancer Letter, June 1).

For this to happen, DePinho needs to receive a conflict of interest waiver from the Board of Regents. In the Q&A, DePinho said he intends to pursue the waiver.

Asked by The Cancer Letter to describe his strengths and weaknesses as an administrator, DePinho required some prompting to get the weakness part.

"Finding ways to be more effective in communicating across many different constituents in such a large and complex organization is something that I need to strive and work for each and every day," he said finally.

If his year of aiming for cancer's gluteus maximus is an indication, DePinho's moon-shooting strategy will continue to create a massive need for explaining how he intends to land his kick on target.

A Year in Houston

Moon Shot "Quite Realistic" Based on Technology Gains

(Continued from page 1)

PG: Of course. What was your answer?

RD: If I recall, just to distill it down to the most elemental points, the major emphasis was that we were entering into an era of science-driven cancer care, in which patients would be administered therapies that would be more effective, based on their genetics, and also avoiding toxicities based on their inherent genetic make-up.

That was an important aspect that permeated most of my comments. I also spoke about the need for increased prevention and early detection.

Prevention is one area that really focuses on understanding why we get cancer in the first place, also developing the right educational tools that enable us to, for example, protect children from sun exposure, to reduce childhood obesity as well as to prevent children each and every day from starting smoking; things of that nature.

Also with respect to early detection, this is where I think some of the greatest near-term impact is going to occur, with the revolution ongoing in serum proteomics and imaging. We have a tremendous opportunity to shift our discovery of cancers to much earlier stages, when the chance for cure is greater.

I place a great deal of emphasis on prevention and early detection.

PG: Would this be what you were going to do at MD Anderson—look at prevention and early detection?

RD: I think in general, the field of cancer has focused significantly on understanding the genetic basis of cancer and focusing significantly on treatment, which is continuing to be a major emphasis for us.

But I mentioned that we are entering into an era where we can be far more proactive in understanding cancer genesis and using that knowledge to prevent disease—look at the revolution that occurred as a result of the HPV vaccine, the knowledge of hepatitis virus, H. pylori.

These are all opportunities for us to understand what drives cancer and intervene in ways that are most effective. I think that the future, while it will continue to focus heavily upon the treatment of advanced disease, will also focus increasingly on preventive-interventive strategies as well as early detection.

PG: So that's your vision for MD Anderson?

RD: Actually, this has been part of our mission for some time. I think it's a matter of emphasis, but it has been central to our mission for many, many years.

PG: Did you get to mention the biotech incubator at that point, or was that not a large enough…

RD: Not yet. But just to finish your first question, the other thing that I also expressed strong interest in, during the interview, was the maintenance of academic excellence.

I talked a lot about mentorship, enhancing our trainee experience, enhancing the ability of our junior faculty to develop sustainable careers, making sure that physician scientists, who wear many hats, are fully supported to achieve the kinds of translational activities that are critically important to drive discoveries into practical endpoints that make a difference for patients.

Your next question?

PG: Was the incubator part of the plans you discussed then?

RD No, but perhaps you mean the Institute for Applied Cancer Science?

PG: Correct.

RD: If you are talking about the Institute for Applied Cancer Science, Giulio Draetta is the director—he was Merck's worldwide head of oncology drug discovery, and prior to that vice president of Pharmacia. The IACS is based on the construct of an institute that started 2003 at Dana Farber called the Belfer Institute for Applied Cancer Science, an institute that focuses on trying to drive discoveries to drug-development endpoints.

It's a new organizational construct that's designed to rigorously validate targets, develop drugs against

those targets, and develop a clinical path hypothesis, so that we can test these novel drugs in the right patient population.

We had some success in Boston, and I was eager to explore similar possibilities on the scale that MD Anderson could provide.

PG: So it's a way of making it bigger?

RD: Not necessarily bigger, but we added some very exciting components to it that in the area of biotherapeutics, whereas in Boston, we were focused mostly on small molecules, so we've expanded into a number of areas.

So the institute supports professional staff that are focused on timelines, deliverables, milestones who work in collaboration with the academic investigators and together move knowledge forward in a very directed way toward drug development endpoints that make a difference for patients.

PG: And so what were the promises that the UT chancellor and the regents made to you, what mandate did they offer?

RD: If you're talking about CPRIT, there were no promises because CPRIT is an independent state agency over which UT System has no control.

PG: Well, I guess what I'm really wondering about is did the CPRIT funds figure into it in any way at all?

RD: I see what the confusion is, because you are going back between UT System and CPRIT.

PG: Correct. I'm not necessarily confused; I mean, I understand the difference…

RD: Because you don't know.

PG: I don't know.

RD: So the Institute for Applied Cancer Science was a construct that we had at Harvard that we wanted to recreate at MD Anderson. That had nothing to do with CPRIT, it was something that was focused on what MD Anderson should do, and that was a discussion that occurred with [UT Executive Vice Chancellor for Health Affairs] Ken Shine and the Board of Regents as a means of bringing individuals down like Giulio Draetta, Lynda Chin [Department of Genomic Medicine chair and IACS scientific director], Phil Jones [head of drug discovery] and others to basically have that same construct be developed at MD Anderson.

So that was a discussion that occurred with the Regents, MD Anderson and numerous individuals. I wasn't involved in the Institute for Applied Cancer Science—that wasn't one of the things that I was discussing with the Regents or with Ken Shine.

PG: You did not? I thought that would be a crucial part of what you would do? Or?

RD: Lynda Chin, Giulio Draetta—they are independent investigators. And in recruiting them down, that discussion was focused on them: where they would have the opportunity to develop their programs that they had in Boston and transplant their activities to MD Anderson.

PG: So that was occurring subsequently to your being offered the job?

RD: Some conversations were simultaneous and some were subsequent. They were all part of the negotiations to try to bring the entire group of individuals down.

PG: I see. So these were different negotiations within the whole process?

RD: They were the typical negotiations that tend to occur between academic investigators and institutions. There is nothing different that was any different from, let's say, us recruiting investigators recently like Sam Hanash, who is now leading a very important proteomics early detection program here, or any different from our recruitment of Jim Allison, where we've invested significantly into our immunology program, or any different from Raghu Kalluri, who is coming down to head our program of cancer biology, or any different from Andy Futreal [professor of genomic medicine], where we made very significant investments in genomic medicine.

PG: When did Dr. Chin's incubator proposal emerge?

RD: Now you're talking about the CPRIT side of the equation.

PG: Right.

RD: Let me put this into a bit of a context. When we came down early on in September, October—Giulio, Lynda, myself, Phil Jones, Eric Devroe [executive director of strategic alliances]—there was great community interest in Houston in trying to understand the Belfer Institute.

There was also great interest in starting biotechnology industry in Houston, and so many individuals asked us to talk about matters of translation, commercialization, and some of these novel constructs.

During the course of those months, there were numerous presentations that were made—I must have made personally at least three or four in which we had many components of the Houston community listening to our presentations.

PG: When was Dr. Chin's incubator merged with rest of the…

RD: I'm leading to that. At that point, there were

individuals who came to us from CPRIT that were extremely interested in what we were talking about and recognized a proposal that had been submitted to CPRIT by Rice as an incubator. Rice had an excellent infrastructure; they had a very good proposal, but they didn't have content for that incubator—something that we generate through the IACS—the content to incubate assets for ultimate commercialization.

And so, the idea was proposed by CPRIT that we should join forces with Rice. I believe those discussions occurred in late November, early December. We were then alerted to the fact that there was this request for proposals in the incubator commercialization group for a component of CPRIT.

The leadership of the institute, which was Guilio Draetta, Lynda Chin, Eric Devroe and Phil Jones, got together with the Rice colleagues, and, under the guidance of the commercialization team at CPRIT, organized this cohesive entity. And that took about two to three months of planning and back and forth, all under the guidance of CPRIT.

PG: I've seen that e-mail from CPRIT, which I got under the Texas freedom of information law, and it appears that that Charles Tate, who's a member of CPRIT oversight committee and commercialization board, is being mentioned as playing a role in devising the application. What role did he play in this process?

RD: I think that that's a question you need to ask CPRIT. I don't know. My understanding is that he is involved on the commercialization side of things, but to my understanding, I do not know of any role that he played, but I would ask that you ask CPRIT or ask Charles Tate himself.

PG: I will, of course. But there were no conversations between you and him?

RD: No one even knew about the institute until we started talking about it after we were here on the ground at Texas and then months after that, this request for consideration that we would merge with Rice emerged. And then we went through the process under the guidance of CPRIT to eventually file the grant.

PG: Does the governor's office plays a role, or lieutenant governor, or the legislature in what you are trying to accomplish in MD Anderson?

RD: No direct role as it relates to our CPRIT funding, but because MD Anderson is a state institution, we do receive crucial funding from the State of Texas to eliminate cancer, which is what we're trying to accomplish at MD Anderson.

The governor did visit MD Anderson to celebrate the opening of the Institute for Applied Cancer Science early on.

There was a major press conference for that, but none of the individuals were involved in any way with the incubator proposal. The Institute for Applied Cancer Science staff submitted a document that was requested in the Request for Applications, and that is what occurred.

PG: The MD Anderson proposal for the incubator is less than seven pages long, and it was funded to receive $18 million three weeks later. It's sort of unusual, did that in any way surprise you that it was so quick and so successful?

RD: I wasn't involved in the detailed aspects of timing and things of that nature.

As the chancellor's external report reviewed, there was a very specific timeline of activities that occurred. The grant was submitted, it was reviewed by an external review team from outside the state and then the recommendation went to the oversight committee and it was recommended for funding.

With respect to the length of the proposal, my understanding is that CPRIT gave very clear guidance on the nature of the proposal and what was to be in the proposal. Second, the point about it being a lot of support—as you know, cancer drug development is extremely expensive—you might know that it takes on average between $15 and $40 million dollars in industry for a single Investigational New Drug, on average, collectively per IND about 140 FTEs [full-time equivalent].

So the drug discovery and development process is very expensive if you are trying to develop lead clinical candidates as opposed to research tool compounds.

PG: Since you have withdrawn this proposal and you are now resubmitting the document, what would it look like, and will you be resubmitting it for scientific review as opposed to just commercialization?

RD: First, I'm sure it's going to be a very, very strong and compelling proposal—the progress in the institute has been quite impressive.

Although we didn't withdraw the original document, we did offer to resubmit and will do so. We are waiting for the revised commercialization request for proposals now and I'm confident that the IACS leadership will respond fully and creatively with a proposal that demonstrates the expertise, the intellect and resources that we have at the institute.

PG: So it will be longer than seven pages this time around.

RD: I actually don't know. I think we're waiting for the guidance from CPRIT, but I'm not involved at that level.

PG: Will it go through a scientific review as well, or?

RD: My understanding is that there are going to be commercialization and scientific review. You may want to check with CPRIT.

PG: I will.

RD: I think it would be an extremely welcome and healthy way of reviewing the grant, but I'm not familiar with the guidelines at this point or what the content of the grant would be.

PG: Well, let's just be done with the incubator, but I guess the more interesting question is, what role does the institute play, within MD Anderson structure? And what role does Dr. Chin's scientific vision play at MD Anderson now?

RD: First of all, Dr. Chin plays a very important role, just as all of our department chairs do. She is chair of a new department of genomic medicine, and her focus is on genomics at a precise moment when technology and scientific thought, concepts, are coming together to cause major disruptive change in the way that cancer is viewed and treated.

She'll sink or swim on her own scientific merit and accomplishment here. I have great confidence in her ability to succeed, as evidenced by her track record, her stature in the field and her publications, including her recent Cell paper that just came out.

In the institute, she is the scientific director and she is one of the leadership group under Giulio Draetta, along with Phil Jones, Jannik Andersen [senior associate director of drug discovery], Joe Marszalek [senior associate director of target validation] and others that are in the leadership group that help manage the myriad activities that occur in the institute.

PG: It must be really challenging to work closely with one's spouse. How is that working out for you?

RD: We have always been bound together by our common interests, not just in our family lives, but in our scientific lives and it's been a tremendous source of, what's the right word… Well, it has just been a very gratifying experience to share a common passion.

So, we have always been able to work very effectively together, because while we work in the same area, we emphasize different things. I'm more of a cancer biologist and geneticist, whereas Lynda is more focused on genomics. And I also work on aging and she doesn't work in that area.

PG: At this point, it's just a potential for, basically, side conversations—and just the difficulty of managing the potential conflicts and appearances of conflicts.

RD: Anybody that's in the room for a few minutes with each of us recognizes that we actually spend very little time talking about science.

With three young children, we tend to focus most of our energies on raising our kids whenever we do have time together. We had, over the years, joint lab meetings—that's where most of the professional interaction is.

Just to give you an example of how little we do communicate on the scientific level, it came as a surprise (to me) that Lynda had a paper published in Cell. And the way I found out about it is that MD Anderson had a press release today and I read the press release and I saw Lynda's name in it and I'm reading on it, and I thought maybe she was commenting on another group's paper, and it turns out that it was her paper in Cell.

So we are independent, we are colleagues, and we do have a lot of common interests scientifically—but we don't spend a lot of free time together on our jobs. In the time that we do spend together, we tend to focus on family, our children and each other.

PG: I understand that you've said in the past that you made a financial sacrifice to come to MD Anderson, is that correct?

RD: I have never said that I have made a financial sacrifice.

I have said that I've made a sacrifice or a personal sacrifice and I feel very honored and privileged to be the leader of MD Anderson, an extraordinary institution that each and every day does amazing things for many, many thousands of patients here and around the world.

PG: What was the sacrifice?

RD: To put it in perspective, Lynda and I spent four years renovating our dream home in Brookline, Massachusetts, and we were a few months away from completion, when the call came to lead this great institution. We felt that the choice, really…that that option took precedent over any personal challenges that we might have.

Also, our three young children were happy in school with their friends, they were thriving, and Lynda's career was going very well. We had a very large support network of both of our families and relatively near in New York City.

Dismantling all of that, particularly uprooting our children, was not easy but leading an institution

such as MD Anderson is a tremendous honor and we're delighted with the career choices we've made. We've had the most fulfilling year of our lives, the children are amazingly adaptive, the schools in Houston are extraordinary, the arts wonderful. The quality of life here is spectacular.

It's a vibrant city with great culture; great personality, and we feel very welcomed in Houston and it's been a very, very gratifying experience overall. And I feel blessed, and I guess that's all I have to say about on that matter.

PG: What were some of the business interests which you have that—investments and equity stakes in companies—that you had to give up or sell? How were those decisions made, about what stays and what goes?

RD: Sure. I have made a complete disclosure to the UT System and also to the Texas Ethics Commission, so you are free to look at that public information if there's anything specific.

But on a high level, I eliminated my role in a number of companies that I was advising them in, due to the limitations of time and the need for intensive focus in the job that I now have the privilege of having.

The only companies that I elected to remain on were companies that I felt I was playing a special role that was essential for the success of the company, and by extension, where my role would help the companies succeed so that they could help patients.

The three companies were AVEO Pharmaceuticals, which is a company that Lynda and I co-founded over ten years ago. It's focused on the development of drugs using sophisticated genetics and cancer biology as well as mouse model systems.

The other one was Metamark Genetics. Again, we were co-founders of that company and that company is focused on diagnostics to develop diagnostics for individuals with prostate cancer, to identify which men are at risk for the development of lethal disease in that context as well as in other cancers such as melanoma.

The third is another company that I was a co-founder is Karyopharm Therapeutics, which is focused on targeting nuclear export machinery as a novel therapeutic approach for cancer.

PG: And you got rid of?

RD: Again, the complete list of a few companies should be in the released documents, but to name a few, I eliminated my role as an advisor for GSK, for Epizyme, for Agios, for Enzon, amongst others, although I still have some equity from my service in Agios and Enzyme.

PG: And the reason is that they could do well without you, they didn't need…

RD: That's right. I was not a founder of those companies. I was merely playing a role as an advisor, and the question that I ask myself with anything that I eliminate or retain is, would it impact adversely on the ability of those companies to impact human health.

PG: So it was basically your own decisions, I suppose, with no feedback from the UT System?

RD: That's correct.

PG: You were able to make the proposals—this is how you're going to deal with the conflicts and they said, fine?

RD: Yes. And they have very strong conflict management procedures that are in place and we could give those procedures to you.

PG: I would love to see them. Recently there was some press coverage of AVEO trial that was proposed for MD Anderson [http://www.chron.com/news/houston-texas/article/M-D-Anderson-involved-in-trial-of-drug-marketed-3711441.php]. Do you think, in retrospect, that it would have been better not to go forward with that study, which of course required you to seek a waiver for it to continue? Are you still seeking a waiver?

RD: First of all, there has been a recent story in the press and we've been successful in correcting some of the misinformation in that story. We have not gone forward with the proposed AVEO study and it will not go forward until we receive guidance from UT System on the conflict issues.

Also, no waiver has been requested with respect to this specific proposed AVEO study. A general waiver of certain provisions of MD Anderson's Conflict of Interest Policies as they pertained to a number of companies, including AVEO, was submitted to UT System. Hand in hand with the waiver request was a detailed proposed plan to monitor and manage conflicts of interest if the waivers were granted.

Shortly after we became aware that AVEO issued a news release incorrectly implying that the study was open at MD Anderson and that a member of MD Anderson's faculty was the lead investigator, we asked AVEO to clarify the release, as it would not be possible for the lead Principal Investigator to be at MD Anderson even if UT System granted the pending waiver, because of other rules that we have that manage conflicts of interest. It's important to understand that those discussions between AVEO and MD Anderson started, I believe, in 2009. This was a number of years before the job for MD Anderson president even

emerged. But at this point, the trial will not open at MD Anderson unless the waiver is approved by UT System.

PG: So you're still seeking the waiver?

RD: Yes. Absent a waiver, AVEO is unable to sponsor any research if the principal investigator is at MD Anderson.

PG: Right. With waiver requests, or one single waiver?

RD: One single request has been sent to UT System, but it includes multiple waiver requests and is not exclusive to this trial or to AVEO, and it includes a comprehensive conflict management plan depending on the company and type of trial involved. For instance, there are different rules depending upon whether the trial involves patients or not.

PG: Are you still aiming for the goal you called the moon shot? And does it still mean curing five cancers in five years, and is it sort of clear which of the cancers will be chosen, and when will this be rolled out?

RD: Well, I don't know where you got the "cure in five years" information from, we are…

PG: I think it was from one of your speeches. If it has changed, that's fine.

RD: No, no it hasn't changed ever. I think it would be rather unrealistic that we would be able to cure cancer in five years.

PG: Or five diseases.

RD: So that we are extremely clear on that one point.

What I have said is that we have reached a point where there is a confluence of technological advances and significant conceptual breakthroughs and clinical proof of concept, such has harnessing the power of the immune system, affecting cell cycle, altering apoptotic responses, and a variety of other hallmarks for cancer where we have drugs that target those hallmarks result in clinical responses, some of which are quite dramatic, that puts us in a position to say that if we organize ourselves in a comprehensive way, in an integrated way, from prevention to early detection to prognostication to treatment and survivorship and recurrence, that we can significantly reduce mortality in this decade for certain cancers.

There are some cancers where we're showing very impressive progress that if we apply what we already know today in a way that is translated and reduced to practice to help patients; in the area of early detection, for example, or in the area of combining very potent drugs with very significant clinical responses, that we will dramatically reduce mortality in those cancers. I can give you a specific example or two, if you'd like.

PG: I'd love to hear which cancers you are targeting.

RD: We're actually going to have a review process from an internal and external advisory group, in fact, tomorrow and the next day, and that will allow us to prioritize these cancers.

We'll initially select up to five cancers, inaugural programs, that we feel that we can put a team on the field that the knowledge in that particular area which is positioned for significant progress—diseases where we have great model systems, enough genomic information, drug interventions where we have significant responses in a proportion of patients that we can build on these current successes and make significant advances.

So based on those guiding principles, we will have selected inaugural programs, but the exercise of going through this strategic planning has set the stage for ultimate cure in the decades ahead, that what we are focused on is trying to develop a strategy for all of the major cancers that we're focused on here, and for those that are not selected, this process will have identified areas for strategic investment at MD Anderson and our collaborators around the country and around the world to work together towards organizing this significant effort that leads to impact on patient survival.

PG: So what's the target of when this will happen and which cancers…?

RD: We will make an announcement in September around the 50th anniversary of Kennedy's moon shot speech which occurred here in Houston in 1962 and it's an aspirational effort that, I think, is quite realistic based on the technological advances and based on the tremendous progress that we've made in the field in a number of cancers.

PG: What's the target date to have these cancers, if not eliminated, controlled?

RD: I think it would be very difficult to answer that question. I think nobody knows the answer.

PG: You do not have that date?

RD: No, of course not, I think it's just not possible to know that. But I do think, and I'm sure you would agree, that we've reached a significant turning point in history of the field. Let's take melanomas for example.

In melanoma, if one applies across a broad front, strategies and prevention, detection, and treatment advances, we believe that we can make significant reductions in mortality. In the area of prevention,

we now know that excessive sun exposure during childhood leads to a dramatic increase in the incidence of melanoma in your 30s and 40s.

So one effort would be to implement educational programs in our schools in much the same we did for traffic safety with seatbelts, and ensure that children and their parents learn that they need to be protected from the sun at that vulnerable period in their lives.

PG: But that's something that people knew for a long time, and do you need MD Anderson to tell you that?

RD: The educational programs that exist in this country are highly fragmented and of course, we'll work with the entire system but what we want to do is inspire our schools to have that as part of their curriculum and to organize the information needed—the public service announcements and the educational materials so that we can move forward on that front. MD Anderson does happen to be the most significant distributor of educational material to oncologists in the world and we would continue that effort in this particular context.

And here I'm giving you just a very specific example. In the area of prevention you would really focus on ensuring that there's good sun protection at a very early stage in life.

Secondly, with respect to early detection, we know from a pilot screening program in Germany that a seven-year screening effort resulted in a 50 percent reduction in mortality because you are catching these cancers at an earlier stage where the chance for survival is much greater simply by surgical excision.

With regard to early detection, there are also major advances in optical imaging, recognition software that is being developed as we speak to enable us to more rapidly identify skin lesions that would allow us to move forward on, and much improve early detection efforts. There are also major diagnostic advances in early-stage cancer in melanoma that enable stratification of cancers that are hardwired to progress to lethal metastatic disease. Such prognostic determinants are being developed that allow us to stratify patients into aggressive versus more benign treatment paradigms.

And then, lastly in the area of therapeutics.

The year 2009 brought truly historic advances on the treatment level, and here the discovery of the BRAF mutation in 2002 from Michael Stratton and Andy Futreal, who's now at MD Anderson, and the development of the drugs squarely directed against that signature mutational lesion has led to a very significant increase in the survival of patients that have that specific event.

In addition, a truly historic event occurred from the work of Jim Allison, also another recent faculty member, who discovered why the immune system is dampened in the context of cancer.

As you know, cancers are not recognized well by the immune system—they appear to be sequestered from the immune response—he discovered a molecule, CTLA-4, that puts the brakes on the immune system, developed the drug against that (anti-CTLA antibody), and now it appears that one in four patients are alive at five years as a result of that treatment.

So let's say we pick melanoma as an inaugural program—we haven't made this decision yet—we would organize our efforts across the broad front involving aggressive educational programs with our school systems, new imaging modalities that more accurately identify early-stage lesions and new prognostic determinants to identify which lesions are hardwired for lethal progression and finally build on the tremendous therapeutic successes since 2009, with BRAF inhibitors, with anti-CTLA antibodies, some of the newer immune modulating drugs like PD-1 which are showing very exciting results in early trials.

With all of those integrated efforts—it's easy to imagine that the now 25 percent survival rates of advanced melanoma and the impact of the mortality that we now have could easily rise to 50 percent within this decade as a result of those comprehensive activities that apply existing knowledge.

PG: Does CPRIT have a role in this?

RD: Well, CPRIT certainly would have a role from the standpoint that part of the way that we're going to be funding this is through a combination of philanthropy as well as through grants from foundations as well as through a number of other federal grants.

PG: I understand that you have told the clinical department chairs at MD Anderson that they would have to boost revenues by another 10 percent. Is that correct?

RD: Yes. The clinical divisions have been asked, as in recent years, for an activity of volume increase ranging from five to 10 percent.

But this is for a division as a whole. We have more faculty each year to accommodate these volume

increases, so the number of new patients seen by any individual faculty will be no higher than what's achieved in many previous years.

We do target a modest increase of two to three percent in patients seen per provider as we seek to become more efficient over time and enhance, for example, IT capabilities, etc. And we always adjust the number of new patients expected to be seen by the faculty members' stated clinical commitment.

PG: Will you increase the percentage of salary and grants to basic scientists? I think it was 30 percent and I believe it's going up to 40?

RD: In 2006, John Mendelsohn [professor of experimental therapeutics and immediate past president of MD Anderson] and Margaret Kripke [professor of immunology emerita and former executive vice president and chief academic officer of MD Anderson] had an external group review of our research. One of their recommendations of the Washington Advisory Group was to increase the salary on grants, which at 30 percent, was significantly lower than comparable institutions.

That was increased to 40 percent in 2011.

Investigators were given about two years advance notice. I wouldn't rule out further increase, but let's remember, at many places, it is north of 80 percent, so this is something we'll evaluate over time.

We also have an incentive plan, and if someone garners more than 40 percent, they get resources back—I believe it is still a very generous arrangement and it helps us both with retention and recruitment.

PG: I hear some of your staff tell me that there's a great deal of excitement at MD Anderson, but directors of other centers and cancer hospitals are telling me that they are recruiting aggressively on the clinical side at MD Anderson and some are successful. Does this worry you that you are losing a lot of staff or some staff?

RD: I believe that we have the most outstanding clinical staff that has been assembled anywhere. It has not been surprising that we do lose some wonderful people to other fine institutions so that they can lead other great institutions, but the number recruited away is small when you consider the critical mass of expertise assembled here.

We have 19,000 employees. Nonetheless, we fight hard to keep as many who are offered elsewhere. We do our fair share recruiting as well and this has been an extraordinary year in recruitment. And so that's more or less what I have to say about that.

PG: I guess you've stepped on some toes this year and you have stepped on a few landmines as well. What do you think are your strengths and weaknesses as a manager of such a massive institution?

RD: I'm having the time of my life. I'm new at this job and I believe I'm learning and growing every day and I suspect I'll continue to learn and grow for the next decade or so.

I think I'm open and direct and I try to be respectful of everyone I work with. I probably try and pack quite a bit into each day—perhaps too much, but I also want to see my children for breakfast when I can.

John Mendelsohn and both his predecessors were all amazingly successful during their tenures as president, and that's the great strength of MD Anderson.

PG: What about your strengths and weaknesses as a manager?

RD: Well, we now are, once again, ranked number one as the best cancer hospital. We have had our most successful year financially in its history. We have successfully recruited a number of extraordinary faculty and administrators. We are number one in NCI grants; we're competing very effectively.

The largest number of high-profile papers in the history of the institution—Cell, Science, Nature, New England Journal of Medicine, and other journals of note—I think that we're doing well as reflected by the progress that we've made in the institution.

PG: Was there a humbling moment—I have one every week, on a good week. Was there anything that you wish you had done differently?

RD: I think that a greater level of communication with respect to how the CPRIT episode was handled—would it have been better perhaps if they'd been more proactive to really explain what occurred factually. We attempted to do that again with respect to this recent story on AVEO, but unfortunately the facts were not as, let's say, incorporated into the story.

So I think finding ways to be more effective in communicating across many different constituents in such a large and complex organization is something that I need to strive and work for each and every day.

PG: Well, thank you very much.

In Brief

AACI To Honor Spitz, Rabson At Oct. 15 Meeting in Chicago

THE ASSOCIATION OF AMERICAN CANCER INSTITUTES will present its **Distinguished Scientist Award** to **MARGARET SPITZ** and its **Special Recognition Award** to **ALAN RABSON**, on October 15, during the 2012 AACI/CCAF Annual Meeting in Chicago.

Spitz's award recognizes her scientific accomplishments and contributions to the cancer center and cancer research communities. Her molecular and genetic epidemiology research includes a focus on inter-individual variation in susceptibility to tobacco carcinogenesis.

Spitz was professor and founding chair of the Department of Epidemiology during a 27-year career at MD Anderson Cancer Center. She joined the Dan L. Duncan Cancer Center at Baylor College of Medicine in 2009 to provide strategic direction for its population sciences program.

Rabson's award marks his more than five decades as a pathologist, cancer researcher, administrator and clinical advisor, as well as his discoveries in virology and authorship of more than 100 scientific journal articles. His son, Arnold Rabson, will accept the award on his father's behalf.

Rabson joined NIH in 1955 and became a staff member in NCI's Laboratory of Pathology the following year. In 1975, he was named director of NCI's Division of Cancer Biology, Diagnosis, and Centers, where he served until his appointment as Deputy Director of the National Cancer Institute in 1995.

Following the award presentation and luncheon on October 15, Spitz will deliver a special keynote talk on integrative epidemiology. Previous AACI Distinguished Scientist Awardees are Lee Hartwell, Mary Claire King, Janet Rowley, Stuart Schreiber, Bert Vogelstein, Robert Weinberg and Irving Weissman.

AACI and the Cancer Center Administrators Forum jointly formulated the program for the 2012 AACI/CCAF Annual Meeting.

AACI awarded four **Translational Cancer Research Fellowships**.

The one-year, $50,000 non-renewable grants help insure that qualified applicants from AACI member institutions receive training and experience under the guidance of established investigators who have demonstrated success in their fields of research. The fellowships are funded by Amgen, Astellas, Lilly USA, and Novartis.

This year's winning researchers and their projects are:

• **Scott Bratman**, resident and postdoctoral fellow in the Department of Radiation Oncology at the Stanford Cancer Institute, for the project: "A genomic strategy for residual disease monitoring in non-small cell lung cancer."

• **Shaun Rosebeck**, research fellow in Pediatric Hematology/Oncology at the University of Michigan Health System, for the project: "Deregulated RIP1 protein modifications in B-lymphomagenesis."

• **Hubing Shi**, postdoctoral fellow in the Division of Dermatology at the David Geffen School of Medicine at UCLA, for the project: "A PDGFRβ-EGFR hetero-complex in B-RAF mutant melanomas with acquired resistance to B-RAF inhibition."

• **David VanderWeele**, a fellow in the Section of Hematology/Oncology at the University of Chicago, for the project: "Prostate cancer oncogenesis: one disease or two?"

RICHARD SCHILSKY has been awarded the 2012 **Bob Pinedo Cancer Care Prize** by the **Society for Translational Oncology**.

Schilsky, professor of medicine and section chief of Hematology/Oncology at the University of Chicago Department of Medicine, was recognized for his clinical and research leadership in the areas of gastrointestinal cancers and cancer pharmacology.

This year's Pinedo Prize of $50,000 will be presented at the society's third annual meeting, to be hosted by UNC Lineberger Comprehensive Cancer Center at the Rizzo Center in Chapel Hill, N.C., Oct. 20-21.

Schilsky will deliver the keynote lecture, "Publicly Funded Clinical Trials and the Future of Cancer Care." The lecture will be published by the journal The Oncologist.

Schilsky is past chairman of the Cancer and Leukemia Group B and former chair of the Board of Scientific Advisors of NCI and of the Oncology Drugs Advisory Committee of FDA.

He is a past president of the American Society of Clinical Oncology, an officer of the board of directors of the Conquer Cancer Foundation, and was recently named an ASCO Fellow.

FDA News

Bosulif Approved For Imatinib-Resistant CML

FDA approved **Bosulif** (bosutinib) to treat chronic myelogenous leukemia. Bosulif is intended for patients with chronic, accelerated or blast phase Philadelphia chromosome positive CML who are resistant to or who cannot tolerate other therapies, including imatinib.

Bosulif is a kinase inhibitor that limits cancer cell growth by inhibiting the Abl and Src signaling pathways. Bosulif works by blocking the signal of the tyrosine kinase that promotes the development of abnormal and unhealthy granulocytes.

The safety and effectiveness of Bosulif was evaluated in a single phase I/II clinical trial that enrolled 546 adult patients who had chronic, accelerated or blast phase CML. These patients had disease that progressed after treatment with imatinib or imatinib followed by dasatinib and/or nilotinib, or who could not tolerate the side effects of prior therapy. All patients in the trial were treated with Bosulif.

Efficacy was determined by the number of patients who experienced a major cytogenetic response within the first 24 weeks of treatment. The results for patients with chronic phase CML who had been previously treated with imatinib only (n=266) was 33.8 percent (95% CI: 28.2, 39.9).

With a minimum follow-up of 23 months, 53.4 percent of patients achieved a MCyR. Of patients who achieved MCyR, 52.8 percent had a MCyR lasting at least 18 months. The median duration of MCyR was not reached for these patients.

The MCyR by 24 weeks for patients with chronic phase CML who had been treated with imatinib and at least one other tyrosine kinase inhibitor (n=108) was 26.9 percent (95% CI: 18.8, 36.2). With a minimum follow-up of 13 months, 32.4 percent of patients achieved a MCyR. Of patients who achieved MCyR, 51.4 percent had a MCyR lasting at least nine months. The median duration of MCyR was not reached for these patients.

A low rate of transformation (4 percent, n=16) from the chronic phase to the advanced or blast phase was also observed in patients treated with Bosulif.

In patients with accelerated CML previously treated with at least imatinib, 33 percent had their blood counts that returned to normal range and 55 percent achieved normal blood counts with no evidence of leukemia within the first 48 weeks of treatment. Meanwhile, 15 percent and 28 percent of patients with blast phase CML achieved complete hematologic response and overall hematologic response, respectively.

The most common side effects observed in those receiving Bosulif were diarrhea, nausea, thrombocytopenia, vomiting, abdominal pain, rash, low red blood cell count, fever and fatigue.

Other drugs recently approved by FDA to treat various forms of CML include imatinib (2001), dasatinib (2006) and nilotinib (2007). Bosulif is marketed by Pfizer.

FDA approved **tbo-filgrastim** to reduce the time certain patients receiving cancer chemotherapy experience severe neutropenia.

Tbo-filgrastim is intended for use in adults who have cancers other than blood or bone marrow cancers (non-myeloid malignancies) and are taking chemotherapy drugs that cause a substantial decrease in the production of neutrophils in the bone marrow. This reduction in neutrophils may lead to infection and fever (febrile neutropenia).

Tbo-filgrastim stimulates the bone marrow to increase the production of neutrophils. It is administered as an injection beginning 24 hours after chemotherapy treatment.

Tbo-filgrastim was evaluated in a clinical study of 348 adult patients with advanced breast cancer receiving treatment with the anti-cancer drugs doxorubicin and docetaxel. Patients were randomly assigned to receive tbo-filgrastim, a placebo, or a non-U.S.-approved filgrastim product, a drug that also stimulates neutrophil production by the bone marrow.

The effectiveness of tbo-filgrastim was determined based on study results that showed that patients receiving tbo-filgrastim recovered from severe neutropenia in 1.1 days compared with 3.8 days in those receiving the placebo.

Tbo-filgrastim's safety was evaluated in three clinical studies composed of 680 adults with breast cancer, lung cancer, or non-Hodgkin's lymphoma who received high-dose chemotherapy that reduces bone marrow cells (myeloablative chemotherapy). The most common side effect observed in those receiving tbo-filgrastim was bone pain.

Tbo-filgrastim is manufactured by Sicor Biotech UAB, a member of Teva Corporation.

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