THE CANCER LETTER

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Turmoil in Texas

DePinho's Wife Was Briefed on AVEO Data 11 Days Before He Touted Stock on CNBC

By Paul Goldberg

What did MD Anderson President Ronald DePinho know when he offered self-serving (and bad) investment advice on a CNBC television show?

Buy AVEO Pharmaceuticals, DePinho said during an appearance on "Closing Bell with Maria Bartiromo" on May 18, 2012, plugging the company he and his wife Lynda Chin co-founded.

Records obtained by The Cancer Letter show that on May 7—exactly 11 days before DePinho offered this ill-advised stock tip—Chin traveled to the Boston area to take part in a meeting of the AVEO Scientific Advisory Board as it prepared to present clinical data to FDA.

(Continued to page 2)

Capitol Hill

As Shutdown Nears, House Republicans Press For Deeper Cuts, Repeal of Obamacare

By Will Craft

As of today, Sept. 13, Congress has five legislative days left to avert a shutdown of the government.

Standing on the cliff's edge, a group of House Republicans are maneuvering to force another round of cuts and, in the same piece of legislation, to take funding away from the Affordable Care Act.

House Majority Leader Eric Cantor (R-Va.) is trying to rally House support for a continuing resolution, proposed Sept. 10, that is paired with a measure to defund the ACA, but would allow the Senate to separate the funding of ACA from the funding of the government as a whole.

He is facing opposition from a bloc of 43 House Republicans, who are saying that the continuing resolution as it stands does not link the continuing resolution and the defunding of Obamacare strongly enough.

(Continued to page 8)

FDA News

ODAC Votes 13:0 For Approving Perjeta

The Oncologic Drugs Advisory Committee Sept. 12 recommended accelerated approval for Genentech's Perjeta (pertuzumab) for neoadjuvant treatment in patients with high-risk, HER2-positive early stage breast cancer.

The committee voted 13 to 0, with one abstention.

Perjeta is likely on the way to becoming the first neoadjuvant breast cancer treatment approved in the U.S. and the first treatment approved based on pathological complete response data.

(Continued to page 10)

Chin: I Did Not Discuss SAB Meeting With Dr. DePinho

(Continued from page 1)

In addition to her role at AVEO, Chin is a senior scientist at MD Anderson. The agenda for the May 7 meeting of the AVEO scientific advisory board consisted of three items, The Cancer Letter has learned. "Discussion of TIVO-1," the phase III trial of the company's drug tivozanib, was one of these items. The trial compared tivozanib with sorafenib in 517 patients with advanced renal cell carcinoma.

Investors who followed DePinho's advice would have seen their holdings erode. The company's development program for tivozanib collapsed as FDA noted that survival on the experimental arm was shorter than on the control arm.

Following a scathing review by the agency's Oncologic Drugs Advisory Committee, the FDA rejected the application.

An updated timeline appears on p. 6.

"I did attend the May 7, 2012 AVEO Scientific Advisory Board meeting," Chin said in an email, responding to questions from The Cancer Letter. "Due to SAB confidentiality requirements, I am unable to disclose confidential or proprietary AVEO information; you may wish to contact AVEO for further information."

DePinho had said previously that he wasn't aware of FDA's views on the approvability of the AVEO drug tivozanib when he appeared on CNBC (The Cancer Letter, May 10, 2013). "I was not involved with the discussions with FDA," he said to The Cancer Letter in May. "I suggest you contact AVEO."

DePinho's assertion that he wasn't aware of problems with the tivozanib data would hold true only if DePinho and Chin didn't talk about business. This is, in fact, what Chin said in response to questions from The Cancer Letter: "I did not discuss the SAB meeting in question with Dr. DePinho."

Schedules Tell the Story

The May 7, 2012, meeting of the SAB preceded AVEO's pre-New-Drug-Application meeting with FDA.

The pre-NDA meeting is easily the most important exchange an applicant has with the regulatory agency, and most companies draw on the expertise of members of their scientific advisory boards in preparation for these meetings.

The meeting with the agency occurred prior to DePinho's May 18 appearance on CNBC, The Cancer Letter reported earlier.

A few days before the meeting, AVEO would have received a letter from the agency, in which regulators described their concerns about the tivozanib application.

The issues on the table at that meeting were profound. Survival data trended in the direction of lower survival for patients who received tivozanib. This trend—though not statistically significant—would ultimately lead to denial of the NDA. The agency doesn't require statistical significance when it considers safety signals.

An individual intimately familiar with the tivozanib data said to The Cancer Letter that the negative survival trend on the experimental arm was visible for months and would have been present at the time the data and safety monitoring board unblinded the data.

The data were reported to AVEO after the study met its primary endpoint, a delay in disease progression. According to a statement Jan. 3, 2012, survival data were said to be not yet mature at the time, and they weren't reported for months that followed.

The trend on overall survival didn't flip to positive, which was noted when the application was scrutinized by ODAC May 2 (The Cancer Letter, May 3).

"A pre-NDA meeting was held in May 2012," FDA reported in the briefing document it prepared for the ODAC meeting. "Here, the FDA expressed concern about the adverse trend in overall survival in the single phase III trial and recommended that the sponsor conduct a second adequately powered randomized trial in a population comparable to that in the U.S.," the

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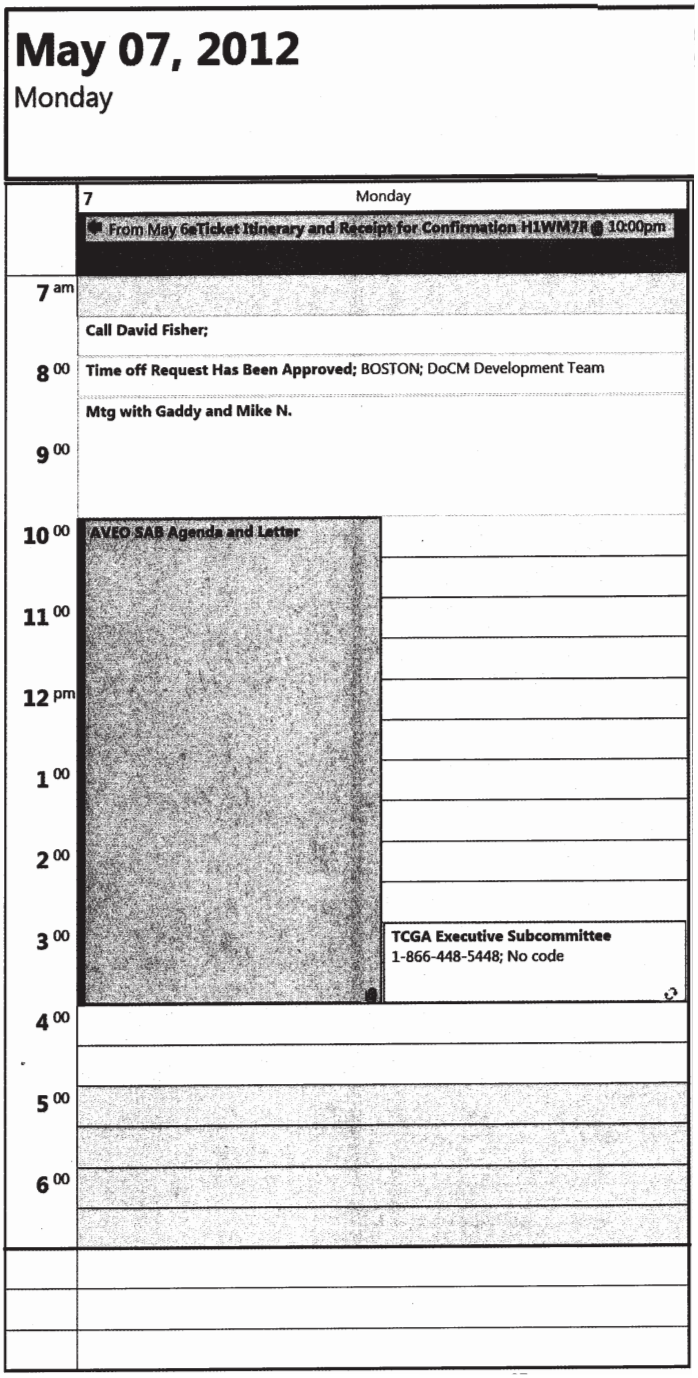
Schedules Tell the Story

Lynda Chin



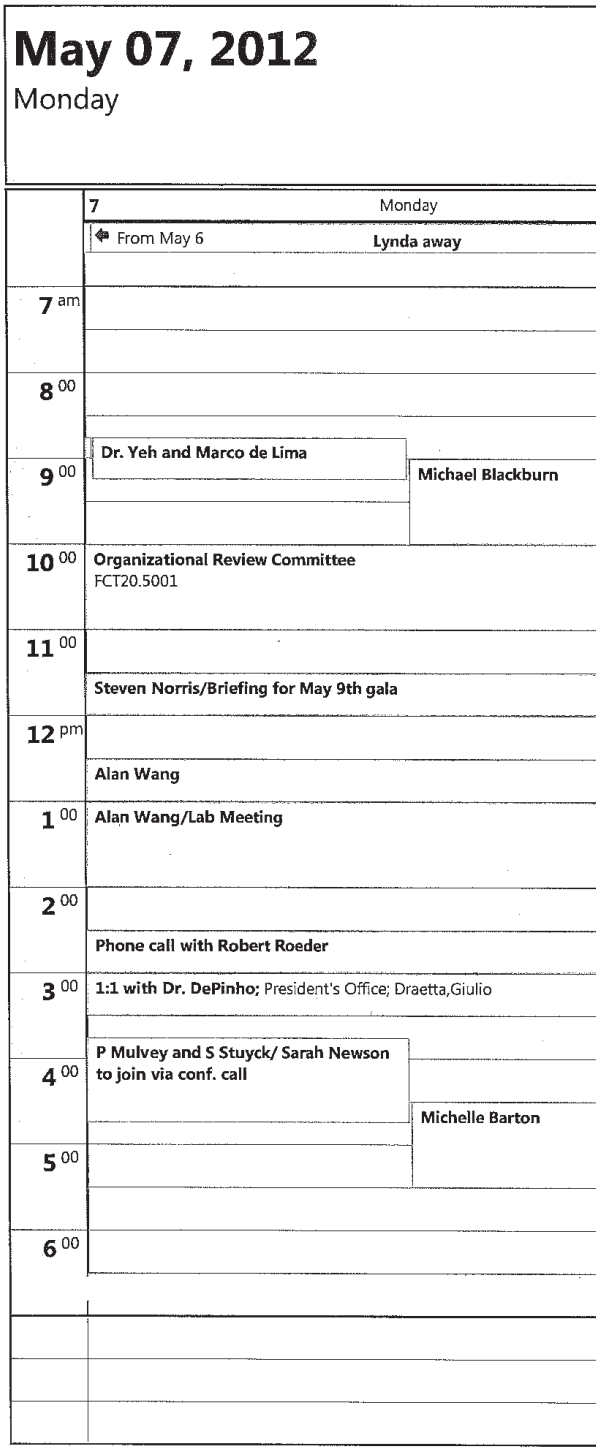
May 07, 2012
Monday

7 Monday

From May 6 eTicket Itinerary and Receipt for Confirmation H1WM7R @ 10:00pm

7 am
Call David Fisher;
8 00 Time off Request Has Been Approved; BOSTON; DoCM Development Team
Mtg with Gaddy and Mike N.
9 00
10 00 AVEO SAB Agenda and Letter
11 00
12 pm
1 00
2 00
3 00 TCGA Executive Subcommittee
1-866-448-5448; No code
4 00
5 00
6 00

Ronald DePinho



May 07, 2012
Monday

7 Monday

From May 6 Lynda away

7 am
8 00
9 00 Dr. Yeh and Marco de Lima — Michael Blackburn
10 00 Organizational Review Committee
FCT20.5001
11 00
Steven Norris/Briefing for May 9th gala
12 pm
Alan Wang
1 00 Alan Wang/Lab Meeting
2 00
Phone call with Robert Roeder
3 00 1:1 with Dr. DePinho; President's Office; Draetta,Giulio
4 00 P Mulvey and S Stuyck/ Sarah Newson to join via conf. call — Michelle Barton
5 00
6 00

agency said (The Cancer Letter, May 10).

Chin's schedule, obtained by The Cancer Letter under the Texas Public Information Act, shows her leaving for Boston in the evening of May 6, 2012. Her time-off request was approved effective the morning of May 7.

The AVEO SAB meeting was scheduled to run from 10 a.m. to 4 p.m.

Chin was double-scheduled to take part in a conference call of The Cancer Genome Atlas executive subcommittee. She was back in Houston on May 8.

DePinho's schedule, which was obtained by the Houston Chronicle under TPIA and made available to The Cancer Letter, states: "Lynda away to May 8."

The claim by Chin that she never discussed the SAB meetings with DePinho is significant for a multitude of reasons.

First, discussion of profound problems with the tivozanib application would have been appropriate, indeed desirable, since DePinho was a member of the AVEO board.

Also, DePinho appeared to be intensely interested in all things AVEO, MD Anderson insiders said.

Sources at MD Anderson said that DePinho was in frequent contact with the company. A sample of the drug, encased in clear plastic, was prominently displayed in his office, insiders said. On weekends, he was seen wearing a jacket with the company logo.

DePinho and Chin had a lot of money riding on the company.

On May 7, 2012, the day of the SAB meeting, their 626,000 shares of AVEO were worth $7.17 million.

Over previous months, the price had fluctuated wildly. For example, on May 11, 2011, the day DePinho was chosen to lead MD Anderson, the family's AVEO stock was worth about $10.6 million.

At this writing, the same number of shares would be worth less than $1.4 million. It's not publicly known how much AVEO stock DePinho and Chin currently hold. Since DePinho stepped off the AVEO board latest year, and the company no longer discloses data related to his trades.

On May 7, 2012, was an important juncture for DePinho and Chin.

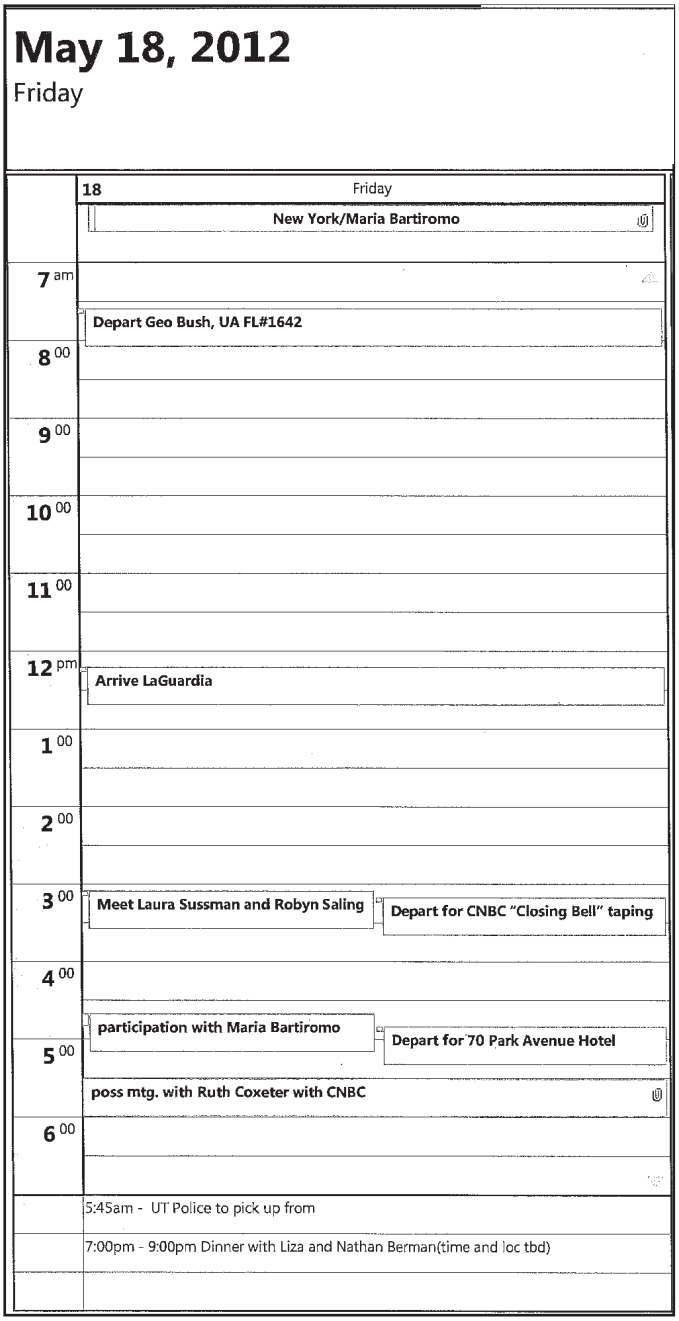
The family's stake in AVEO had the potential to drop precipitously, as it did, because of FDA's position on tivozanib, or it could have recovered the losses and skyrocketed if the drug were obviously heading toward approval.

More than just money was at stake.

The UT System Board of Regents selected DePinho over other candidates for the job of MD Anderson president because of his interest in commercializing pharmaceutical compounds and his promise to make drug development more rational.

Chin, who runs a newly created institute at MD Anderson, took on the role of creating a hybrid of an academic institution and an efficiently run drug company.

Ronald DePinho



May 18, 2012

Friday

	18 Friday
	New York/Maria Bartiromo
7 am	
	Depart Geo Bush, UA FL#1642
8 00	
9 00	
10 00	
11 00	
12 pm	Arrive LaGuardia
1 00	
2 00	
3 00	Meet Laura Sussman and Robyn Saling / Depart for CNBC "Closing Bell" taping
4 00	
5 00	participation with Maria Bartiromo / Depart for 70 Park Avenue Hotel
	poss mtg. with Ruth Coxeter with CNBC
6 00	
	5:45am - UT Police to pick up from
	7:00pm - 9:00pm Dinner with Liza and Nathan Berman(time and loc tbd)

DePinho's schedule the day he offered stock advice on CNBC's Closing Bell with Maria Bartiromo.

Is it possible that MD Anderson's first couple indeed doesn't talk about business? DePinho has said so in the past (The Cancer Letter, Sept. 7, 2012).

Be that as it may, his and her schedules show a lot of travel, but they also show opportunities to talk.

For example, on May 10, 2012, at 5:30 p.m., DePinho and Chin were picked up by UT Police and taken to a dinner and a breast cancer fundraising event at the Brown Theater. The performances were put together by Houston Grand Opera, the Alley Theatre, and the Houston Ballet, which contributed the wedding night pas de deux from Madame Butterfly.

The schedules also provide new insight into DePinho's appearance on CNBC. On May 18, 2012, after landing in New York, he meets with—or is coached by—an MD Anderson public affairs staff member Laura Sussman and outside PR consultant Robyn Saling.

The fact that DePinho is accompanied by an MD Anderson staff member and contractor confirms the company's assertion that DePinho wasn't authorized to speak for the company.

Introduced by CNBC's Bartiromo as MD Anderson president, DePinho says that investors should bet only on companies that are guided by emerging molecular-level insight into cancer.

He briefly mentions Genentech as an example of such a company, and then segues to AVEO.

"A company that I was involved in founding—AVEO Pharmaceuticals, one of the most successful biotechs," DePinho said, is developing "a very effective drug that has a superior safety profile for renal cell cancer, a major unmet need."

A video of DePinho's appearance is available on the CNBC website.

A scientist intimately familiar with the TIVO-1 data was shocked by what he saw on CNBC.

"My reaction was, 'What was he looking at? If it was the same data I saw, I wouldn't be saying it s the greatest thing since sliced bread,'" the scientist recalled.

DePinho's characterization of tivozanib as meeting a "major unmet need," was debatable.

Also, the phrase echoed the term of trade "unmet medical need," which describes the FDA criteria for awarding a Fast Track designation, which allows the agency to work closer with the sponsor to get an important drug on the market.

AVEO officials at the time said to The Cancer Letter that they weren't applying for the designation.

Indeed, with eight drugs already on the market, the renal cancer indication had more treatment options than most cancers (The Cancer Letter, June 1, 2012).

Caplan: This is Why COI Rules Exist

"The very reason for the emergence of COI rules and disclosure requirements is the murky and challenging set of interactions in this story," said Arthur Caplan, the Drs. William F. and Virginia Connolly Mitty Professor and head of the Division of Bioethics at New York University Langone Medical Center. "Who said what to whom and when should be clear, and not merely debated or left to retrospection."

UT System leadership appears to have accepted DePinho's assurances that he didn't know about FDA's problems with the tivozanib application at the time he touted the stock.

"It is our understanding that President DePinho never participated in a meeting between the FDA and AVEO, nor do we have any evidence whatsoever to suggest that he had access to any FDA information at the time of the CNBC interview," UT System Chancellor Francisco Cigarroa said in a statement (The Cancer Letter, May 10).

AVEO said that the Securities and Exchange Commission recently issued a subpoena covering documents related to tivozanib. Separately, the company is facing shareholders' suits. AVEO officials did not respond to questions by deadline.

MD Anderson's COI policy 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."

Of course, the UT System officials knew about DePinho's and Chin's industry involvements.

The conflicts and plans for their management were noted in the offer letters to the couple.

Yet, a formal waiver wouldn't be issued until late 2012, which likely meant that DePinho and Chin operated in violation of MD Anderson's COI policies for more than a year.

MD Anderson officials said that a blind trust has since been established to manage some of the couple's assets.

"The transfer of assets to the blind trust is in progress," MD Anderson officials said in a statement.

The Tivozanib Timeline

December 2008, May 2009

End-of-phase II meetings between AVEO Pharmaceuticals Inc. and FDA result in agreement concerning the design of the phase III trial of tivozanib for advanced renal cell carcinoma.

During the December 2008 meeting, the agency and AVEO discuss several study designs and FDA states that "a substantial, robust improvement in PFS that is clinically meaningful and statistically persuasive may be considered for regulatory decision."

FDA also states that "a statistically significant improvement in OS is not required for regulatory approval, but a pre-specified OS analysis plan is still helpful in the regulatory decision making process."

In the May 2009 meeting, the agency and AVEO discuss the final phase III protocol. Crossover design is not discussed and is not included in the phase III study itself (a later protocol added the crossover). See the FDA briefing documents for ODAC.

According to clinicaltrials.gov, the study's estimated completion date—defined as final collection date for primary outcome measure—is December 2011.

June 9, 2011

Ronald DePinho, co-founder of AVEO and member of the company's board of directors, is named president of MD Anderson Cancer Center. His wife, Lynda Chin, an AVEO co-founder, joins MD Anderson as a senior scientist.

April 16, 2012

AVEO says the TIVO-1 pivotal trial demonstrates tivozanib's safety and efficacy. In a press release, William Slichenmyer, the company's chief medical officer, states: "We believe that the efficacy and safety profile consistently demonstrated by tivozanib and recently validated in our phase III TIVO-1 trial represent an important step forward in the treatment of patients who have advanced RCC. We are pleased with the opportunity to collaborate with tivozanib study investigators on publishing these positive phase II data in the Journal of Clinical Oncology, and look forward to advancing our work with our global partners at Astellas to bring tivozanib to patients who can benefit from this therapy."

April 20, 2012

DePinho asks for a waiver from the UT System to allow him to stay involved in commercial activities. The waiver would cover his service on the board of AVEO (The Cancer Letter, Oct. 26, 2012).

May 7, 2012

AVEO holds a meeting of its Scientific Advisory Board. The results of tivozanib trial are on the agenda.

Mid-May, 2012 (prior to May 18)

At the pre-NDA meeting, FDA officials say the agency "expressed concern about the adverse trend in overall survival in the single phase III trial and recommended that the sponsor conduct a second adequately powered randomized trial in a population comparable to that in the U.S."

According to the agency, the final analysis of overall survival showed a trend toward a detrimental effect on OS with tivozanib; HR=1.25, p=0.11. Median OS was 28.8 months in the tivozanib arm and 29.3 months in the sorafenib arm. See the FDA briefing documents for ODAC. The agency declined to release the exact date of the pre-NDA meeting.

May 16, 2012

An AVEO press release states that "overall survival data are not yet mature." The press release reports progression-free survival data: "Based on independent radiological reviews, tivozanib demonstrated a statistically significant improvement in PFS with a median PFS of 11.9 months compared to a median PFS of 9.1 months for sorafenib in the overall (Intent To Treat) study population (HR=0.797, 95% CI 0.639–0.993; P=0.042). Objective response rate for tivozanib was 33 percent compared to 23 percent for sorafenib. The efficacy advantage of tivozanib over sorafenib was consistent across subgroups in the study."

May 18, 2012

DePinho—who, at the time, was on the AVEO board of directors—appears on the CNBC program "Closing Bell with Maria Bartiromo."

He recommends investment in the company and its drug, stating that AVEO "has utilized, has exploited science-driven drug discovery, and it's about to announce, or has announced already publicly, and will present in detail at ASCO, a very effective drug that has a superior safety profile for renal cell cancer, a major unmet need. So these are massive advances in our ability to really do something about a disease that has long been very refractory."

The appearance is posted on the CNBC website, and a transcript can be downloaded from The Cancer Letter.

DePinho and his family hold 590,440 shares in AVEO, company filings show. For three days preceding DePinho's appearance on CNBC, AVEO's stock price had been falling, trading at $11.28 per share just before DePinho goes on camera. The DePinhos' holdings are worth $6.66 million.

June 1, 2012

Contacted by The Cancer Letter, DePinho apologizes for praising AVEO stock on the CNBC program. Offering investment advice is inconsistent with his position as an employee of the state of Texas (The Cancer Letter, June 1, 2012). Following DePinho's appearance, the share price started to climb back up, trading at about $12.73 when the market closed on May 31, making the DePinho holdings worth about $7.5 million.

June 2, 2012

At the annual meeting of the American Society of Clinical Oncology, Robert Motzer, an attending physician on the Genitourinary Oncology Service at Memorial Sloan-Kettering Cancer Center and the principal investigator on the study, presents the TIVO-1 data. He says the overall survival data would be presented at a later date.

Aug. 2, 2012

AVEO acknowledges the survival deficit. A press release contains a "regulatory update," which states:

"The FDA has expressed concern regarding the OS trend in the TIVO-1 trial and has said that it will review these findings at the time of the NDA filing as well as during the review of the NDA. AVEO is conducting additional analyses to be included in the NDA submission that demonstrate that the OS data from TIVO-1 are consistent with improved clinical outcomes in RCC patients receiving more than one line of therapy; analyses that the company believes will directly address this issue. AVEO is continuing to work toward submitting the NDA by end of the third quarter; however, there is a chance that the additional OS analyses may cause the submission to move into the fourth quarter."

Sept. 28, 2012

AVEO submits an application for tivozanib for the treatment of advanced renal cell carcinoma. According to a press release, the application is supported by a single phase III trial, a randomized phase II trial, and an extension/crossover study.

Oct. 10, 2012

DePinho receives a waiver, which enables him to continue to serve on the AVEO board of directors (The Cancer Letter, Oct. 26, 2012). The waiver requires him to place the stocks of AVEO and other firms in a blind trust.

Dec. 20, 2012

AVEO announces that DePinho would step off the board effective Dec. 31, 2012. His wife, Chin, continues to serve on the company's scientific advisory board.

May 2, 2013

ODAC votes 13:1 against approval of tivozanib, concurring with the agency that a deficit in overall survival on the experimental arm is unacceptable (The Cancer Letter, May 3). Post-ODAC, the company is trading at just above around $2.50, which means that if the DePinho holdings in AVEO remained the same, they would be worth less than $1.5 million.

Capitol Hill

House Continuing Resolution Seeks More Cuts To NIH Budget

(Continued from page 1)

The goal of the 43 Republicans is to make it impossible for the Senate to separate the two measures. If the version of the continuing resolution championed by Cantor is approved by the House, the Senate could vote twice—first, to prevent the shutdown and then to strike down the defunding of the ACA.

By taking this stance, Republicans—particularly conservatives affiliated with the Tea Party—are saying: If you want to keep the government open on Oct. 1 and beyond, lose Obamacare.

The House version of the CR, which would extend funding through Dec. 15, cuts government funds to below the sequester level.

If approved, the federal budget would shrink by $1.7 billion, from the current level of $988 billion to $986.3 billion for the 11-week lifespan of the resolution.

"This is not the preferred way of doing the nation's financial work—this Congress can and should be passing regular appropriations bills that reflect the country's changing fiscal needs and realities," bill sponsor Rep. Hal Rogers (R-Ky.) said in a statement.

"However, given the late date, a continuing resolution is necessary to stop a government-wide shutdown that would halt critical government programs and services, destabilize our economy, and put the safety and well-being of our citizens at risk.

"Our country desperately needs a long-term budget solution that ends the draconian cuts put into place by sequestration, and that provides for a responsible, sustainable, and attainable federal budget. It is my hope that this stopgap legislation will provide time for all sides to come together to reach this essential goal."

Despite the urgency in Rogers's words, Cantor has pushed back a vote on the bill until next week in order to rally the support needed to pass the budget resolution.

The Battle of the Budgets

When the sequester hit, the NIH budget was reduced from about $30.8 billion to $29 billion, a $1.71 billion cut (The Cancer Letter, June 7). Government agencies will be left uncertain as to what their operating budgets will be until a compromise is reached for the new fiscal year.

Obama's proposed 2014 budget would increase NIH funding to $31.3 billion—a nearly 2 percent raise over the 2012 budget, and about 7 percent, or $2.3 billion, above sequestration levels.

The Senate's proposed 2014 HHS budget was marked up and approved July 7, and is now pending a full Senate vote.

The Senate bill provides $164 billion for investments in medical research, reducing healthcare costs, and other programs.

At this writing, the House's version of the HHS budget has yet to be marked up. Republican leaders have said that they plan to exclude funding for the ACA from the legislation.

Several members of the House have issued an ultimatum: either the FY 2014 HHS budget defunds the Affordable Care Act, or they will try to force a government shutdown. Though Appropriations Committee Chairman Rogers opposes a government shutdown, the House has voted to repeal the ACA 37 times.

The House HHS subcommittee announced an appropriation of $121.8 billion in July, but the markup has been postponed indefinitely, according a statement. With the continuing resolution being put forward, it may be months until the release of a full breakdown of the bill.

"The house allocation for the labor HHS bill is more than 18.5 percent below the sequester level of spending," said David Pugach, director of federal relations for the American Cancer Society Cancer Action Network. "If you simply did that across the board, NIH would be cut about $5.5 billion below where it is right now."

If these cuts were applied evenly across the agencies funded through the Labor, HHS and Education spending bill, with inflation taken into account, NIH would have its lowest budget since the 1990's.

However, without a House HHS markup, there is no way to know exactly how NIH would be affected.

A Lasting Impact

Operating on sequester-level funding, many agencies are struggling under the 5.1 percent cuts that their new budgets demand of them.

The cut is actually closer to 10 percent because sequestration began partway through the fiscal year, said Chris Hansen, president of ACSCAN.

The cuts reduced the size and number of grants, lowered the grant success rate, and caused many researchers to slow down and cut back on both research and preventative operations.

"A nuance of how the sequestration works that speaks to its long-term harm is that our NCI

comprehensive cancer center grant was submitted in May for its re-competition," said Donald Trump of the Roswell Park Cancer Institute at an ACSCAN roundtable Sept. 10. "Our notice of grant award came in mid-September.

"And that notice becomes the baseline from which we can compete our new grant, which will be funded again next September, for another five years," Trump said. "But that baseline is 10 percent less than it was last year because of sequestration. And that baseline continues for the next five years.

"You can make up a 4 or 5 or 6 percent deficit in the budget one time, but as it goes on, you begin to really erode the base, you begin to cut into programs. If this continues we are going to have to cut into our scientific programs."

With the NIH grant success rate down to 18 percent, the sequester is causing many young scientists to reconsider a career in research.

"[Young researchers] are struggling big time in our community—our cancer centers," said Edward Partridge, director of the University of Alabama at Birmingham Comprehensive Cancer Center. "We have some very discouraged young investigators that are wondering whether or not they can make a living as a scientist, with great ideas and great minds, but in a tough environment to be successful.

"At 34, 35 years old, they have family, they have been supported for three years by their institutions, and because it's so tough they can't support themselves, so they go to administration, they go to industry—they find another way to make a living."

Also, cancer centers around the country are being forced to cut back on prevention programs, which may be causing the government to spend more money on treatment and aftercare.

"Are we saving money that the sequester is forcing us not to spend?" asked ACS CAN's Hansen. "No, we are spending more money, because you are paying for care for people who have advanced cancers, and that's far, far more expensive than just screening people, and finding it early."

John Seffrin, CEO of the American Cancer Society, said the cuts will harm patients.

"What's different from when I started my career and got involved with the American cancer society in 1972, most of the suffering from cancer today is needless," Seffrin said.

"This suffering didn't need to happen and the deaths didn't need to occur."

Quality of Care

IOM Report Details Nationwide Crisis Facing Cancer Care, Offering Six Main Solutions

A report by the Institute of Medicine recommends a series to help the U.S. maneuver its way out of the current crisis in cancer care.

The 315-page report, titled "Delivering High-Quality Cancer Care: Charting a New Course for a System in Crisis" addresses issues that include meeting the growing demand for cancer care amid rising costs and the increasing complexity of treatment.

"As a nation, we need to chart a new course for cancer care," said Patricia Ganz, chair of the committee that wrote the report, and a professor at the School of Medicine and School of Public Health at the University of California, Los Angeles. "Changes are needed across the board, from how we communicate with patients, to how we translate research into practice, to how we coordinate care and measure its quality,"

"Most clinicians caring for cancer patients are trying to provide optimal care, but they're finding it increasingly difficult because of a range of barriers."

Cancer incidence is expected to rise by 45 percent to 2.3 million new diagnoses per year by 2030. Today, more than 1.6 million new cases are diagnosed each year. The oncology work force may be too small to care for the rising number of people diagnosed with cancer, and training programs lack the ability to rapidly expand, the report said.

The cost of cancer care is rising faster than other sectors of medicine, having increased from $72 billion in 2004 to $125 billion in 2010, the report said. At the current rate, it will increase another 39 percent to $173 billion by 2020.

"For oncologists, continuously improving the quality of cancer care is at the core of our mission. This report provides important strategies we can use now to reach this goal," said Clifford Hudis, president of the American Society of Clinical Oncology. "We commend the IOM for this landmark report and will work with policymakers, patients, health IT groups and the oncology community to implement its recommendations."

The recommendations include:

• **Engaged patients**. The cancer care system should support patients in making informed medical decisions that are consistent with their needs, values, and preferences. Cancer care teams should provide

patients and their families with understandable information about the cancer prognosis and the benefits, harms, and costs of treatments. NCI, the Centers for Medicare and Medicaid Services, and other stakeholders should improve the development and dissemination of this critical information, using decision aids when possible.

• **An adequately staffed, trained, and coordinated work force**. New models of team-based care are an effective way to promote coordinated cancer care and to respond to existing work-force shortages and demographic changes. And to achieve high-quality cancer care, the work force must include enough clinicians with essential core competencies for treating patients with cancer. Professional organizations that represent those who care for patients with cancer should define these core competencies, and organizations that deliver cancer care should ensure their clinicians have those skills.

• **Evidence-based cancer care**. A high-quality cancer care delivery system uses results from scientific research to inform medical decisions, but currently many medical decisions are not supported by sufficient evidence, the report says. Clinical research should gather evidence of the benefits and harms of various treatment options so that patients and their cancer care teams can make more informed treatment decisions. Research should also capture the impacts of treatment regimens on quality of life, symptoms, and patients' overall experience with the disease. Additional research is needed on cancer interventions for older adults and those with multiple chronic diseases. The current system is poorly prepared to address the complex care needs of these patients.

• **A learning health care information technology system for cancer care**. A system is needed that can "learn" by enabling real-time analysis of data from cancer patients in a variety of care settings to improve knowledge and inform medical decisions. Professional organizations and the Department of Health and Human Services should develop and implement the learning health care system, and payers should create incentives for clinicians to participate as it develops.

• **Translation of evidence into practice, quality measurement, and performance improvement**. Tools and initiatives should be delivered to help clinicians quickly incorporate new medical knowledge into routine care. And quality measures are needed to provide a standardized way to assess the quality of cancer care delivered. These measures have the potential to drive improvements in care, inform patients, and influence clinician behavior and reimbursement.

• **Accessible and affordable cancer care**. Currently there are major disparities in access to cancer care among individuals who are of lower socio-economic status, are racial or ethnic minorities, lack health insurance coverage, and are older. HHS should develop a national strategy that leverages existing community interventions to provide accessible and affordable cancer care, the report says. To improve the affordability of care, professional societies should publicly disseminate evidence-based information about cancer care practices that are unnecessary or where the harm may outweigh the benefits. CMS and other payers should design and evaluate new payment models that incentivize cancer care teams to provide care based on the best available evidence and that aligns with their patients' needs. The current fee-for-service reimbursement system encourages a high volume of care, but fails to reward the provision of high-quality care.

FDA News

ODAC Recommends Perjeta For Accelerated Approval

(Continued from page 1)

Full approval—and, likely, the continuation of accelerated approval—would be contingent on the outcome of phase III APHINITY study.

This confirmatory trial is evaluating Perjeta in the adjuvant setting and compares Perjeta, Herceptin (trastuzumab) and chemotherapy with Herceptin and chemotherapy in people with HER2-positive early stage breast cancer.

APHINITY has completed enrollment with approximately 4,800 people, and the primary end point is invasive disease-free survival. Genentech has proposed this study as a confirmatory study to the FDA. Data are expected in 2016, the company said.

ODAC's recommendation was based on two phase II studies, NEOSPHERE and TRYPHAENA, in high-risk, HER2-positive early stage breast cancer, as well as on longer-term safety data from the phase III CLEOPATRA study of Perjeta in HER2-positive metastatic breast cancer.

FDA is scheduled to make a decision by Oct. 31, 2013.

Perjeta is approved in a number of countries, including the U.S., for HER2-positive metastatic breast cancer.

In the NEOSPHERE study, treatment with Perjeta, Herceptin and docetaxel chemotherapy significantly improved the rate of total pathological complete response by 17.8 percentage points compared to Herceptin and docetaxel alone (39.3 percent vs. 21.5 percent, respectively; p=0.0063).

A detailed story on the ODAC discussion and the implications of its recommendation will appear in the Sept. 20 issue of The Cancer Letter.

FDA expanded the approved uses of Abraxane to include the treatment of patients with metastatic pancreatic cancer, in combination with gemcitabine.

Abraxane (paclitaxel protein-bound particles for injectable suspension, albumin-bound) is also approved to treat breast cancer and non-small cell lung cancer.

The safety and effectiveness of Abraxane for pancreatic cancer were established in a clinical trial with 861 participants who were randomly assigned to receive Abraxane plus gemcitabine or gemcitabine alone. Participants treated with Abraxane plus gemcitabine lived, on average, 1.8 months longer than those treated with gemcitabine alone.

Additionally, participants who received Abraxane plus gemcitabine experienced a delay in tumor growth that was, on average, 1.8 months later than the participants who only received gemcitabine.

Common side effects observed in Abraxane plus gemcitabine-treated participants include neutropenia, thrombocytopenia, fatigue, peripheral neuropathy, nausea, hair loss, tissue swelling, diarrhea, fever, vomiting, rash, and dehydration.

Abraxane is sponsored by Celgene. Gemcitabine is marketed by Eli Lilly & Co.

FDA granted priority review for Nexavar tablets under evaluation for the treatment of locally advanced or metastatic radioactive iodine-refractory differentiated thyroid cancer.

Nexavar (sorafenib), an oral multi-kinase inhibitor, is approved in the U.S. for the treatment of patients with unresectable hepatocellular carcinoma and for the treatment of patients with advanced renal cell carcinoma.

Nexavar is thought to inhibit both the tumor cell and tumor vasculature. In in vitro studies, Nexavar has been shown to inhibit multiple kinases thought to be involved in both cell proliferation and angiogenesis. These kinases include Raf kinase, VEGFR-1, VEGFR-2, VEGFR-3, PDGFR-B, KIT, FLT-3 and RET.

Nexavar is sponsored by Bayer HealthCare and Onyx Pharmaceuticals.

FDA accepted a New Drug Application for ibrutinib in two B-cell malignancy indications: previously treated mantle cell lymphoma, and previously treated chronic lymphocytic leukemia/small lymphocytic lymphoma.

The effectiveness of ibrutinib, an investigational oral Bruton's tyrosine kinase inhibitor, is being studied in several B-cell malignancies, including chronic lymphocytic leukemia/small lymphocytic lymphoma, mantle cell lymphoma, diffuse large B-cell lymphoma, follicular lymphoma, Waldenstrom's macroglobulinemia and multiple myeloma.

Janssen Biotech Inc. and Pharmacyclics Inc. entered a collaboration and license agreement to develop and commercialize ibrutinib.

Obituary

Outcomes Research Pioneer Jane Carrie Weeks Dies at 61

Jane Carrie Weeks, a prominent researcher at Dana-Farber Cancer Institute, internationally known for building the discipline of outcomes research in oncology and admired by colleagues as an outstanding mentor, died from breast cancer Sept. 10. She was 61.

She was "one of the true intellectual pillars of the Harvard medical community," said Dana-Farber President Edward Benz, Jr.

Weeks was professor of medicine at Harvard Medical School, professor of health policy and management at Harvard School of Public Health, director of the McGraw-Patterson Center for Population Sciences, and chief of the Division of Population Sciences within the Department of Medical Oncology at Dana-Farber. She also served as the program leader for Outcomes Research at Dana-Farber/Harvard Cancer Center.

Weeks received her medical degree from Harvard Medical School and a master's degree in health policy and management from Harvard School of Public Health. She completed postgraduate training in internal medicine at Brigham and Women's Hospital and in medical oncology at Dana-Farber, joining the faculty in 1992.

This past June, Weeks received a William Silen Lifetime Achievement in Mentoring Award from Harvard Medical School.

At that time, her Dana-Farber colleague and mentee Deborah Schrag said, "Jane asks the critical questions about how we deliver clinical care-questions that have changed the way we think about and practice cancer medicine at its most profound level.

"In addition to her powerful intellect and analytic rigor, Jane is the consummate mentor," Schrag said. "Her trainees now populate the field of health services research in oncology across the country."

In 1995, Weeks founded Dana-Farber's Center for Outcomes and Policy Research. She was an influential scientist in the field of outcomes research, which focuses on the benefits, risks, and results of treatment and takes into account patients' experiences and preferences.

She published more than 200 scientific papers on a broad range of topics related to cancer prevention and treatment, cost-effectiveness of health services, racial disparities in health care and patient preferences about end-of-life care.

Weeks was a pioneer in comparative effectiveness research, which addresses the reality that many decisions about cancer treatment must be made with imperfect evidence.

While clinical trials can provide some answers, Weeks built other resources that brought together a broad array of clinical data and included the perspectives of patients and their families.

Among her leadership roles, Weeks led the Cancer Care Outcomes Research and Surveillance Consortium, a six-year study funded by NCI, which examined the experiences of 10,000 patients from across the U.S. throughout their treatment. The study searched for clues as to why some groups, such as the elderly and minorities, sometimes receive lower-quality care or achieve inferior outcomes.

Weeks is survived by her husband, Barrett Rollins, the Linde Professor of Medicine at Harvard Medical School and chief scientific officer and faculty dean for oncology at Dana-Farber Cancer Institute.

Memorial services are being scheduled.

In lieu of flowers, gifts may be made to the Jane C. Weeks Junior Population Science and Clinical Investigator Endowment Fund. To make your gift online, please visit: http://www.dana-farber.org/janeweeks.

To give by mail, please send a check payable to Dana-Farber to: Dana-Farber Cancer Institute and the Jimmy Fund, 10 Brookline Place West, Brookline, MA 02445, noting "Jane Weeks Fund" in the memo field. Gifts may also be charged by phone by calling the Development Office at 617-632-6099.