THE CANCER LETTER

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Cancer Communications: The Cost

NIH Spent $181.3 Million on PR Last Year; House Probe Prompts Analysis of Spending

By Paul Goldberg

A Congressional investigation of spending on public relations has forced NIH to do something it hasn't done before: tally such expenses across the institutes and centers.

The total they got may strike some as excessive, even shocking.

Altogether, the NIH units spent $181.3 million on work that can be broadly characterized as PR in fiscal 2012, officials said in a detailed response to questions from investigators at the House Committee on Appropriations and the Committee on Energy and Commerce.

The document wasn't intended for dissemination to the public, but a copy was obtained by The Cancer Letter and is posted on the website.

In his letter to Congress, NIH Director Francis Collins pointed out that this sum accounts for less than 0.6 percent of the $30.9 billion taxpayers spent on biomedical research that year, and that many public information activities are, in fact, required by law.

"There are more than 55 provisions within the Public Health Service Act that authorize the NIH to disseminate health information and conduct and support public education activities, such as clearinghouses, awareness programs, and public engagement efforts," Collins said in a cover letter that conveyed the detailed answers to House investigators.

The 59-page response from NIH breaks down PR spending to show spending by each of the NIH units. A list of major contractors and the magnitude of their contracts is provided for every institute and center. Also listed are the mandates for each NIH unit to engage in communications.

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Turmoil in Texas

SEC Issues Subpoena to AVEO on Tivozanib

By Paul Goldberg

AVEO Pharmaceuticals Inc. said the Securities and Exchange Commission has subpoenaed documents related to its drug tivozanib.

The company co-founded by MD Anderson President Ronald DePinho made the announcement in an SEC filing on July 11. The subpoena was received eight days earlier, the filing stated.

Last year, DePinho recommended the company's stock on a CNBC program. The appearance post-dated a meeting between AVEO and FDA at which the regulatory agency told the company that the trend toward lower

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NIH Didn't Know Spending Level Until Congress Asked Questions

(Continued from page 1)

The Congressional investigation was triggered by The Cancer Letter's series of stories on the cost of cancer communications.

Figures show that in fiscal 2012 NCI was the biggest spender on PR at NIH, with the total budget of $46.2 million. This amounts to 26 percent of the aggregate NIH spending on these activities.

This level of spending by NCI actually represents a decrease. In years past—from fiscal 2006 to 2012—the budget of the institute's Office of Communications and Education added up to $381.2 million. In 2006, the OCE budget stood at $68.1 million (The Cancer Letter, March 1).

Last year, the NIH Office of the Director was a distant second largest spender among the institutes and centers—with a $21.8 million budget split between a large number of activities.

NCI's public relations and education budget is also roughly double that of FDA's PR operations that support health and medical programs. These offices run vitally important communications about outbreaks of disease.

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Massive Number, Massive Challenge

The release of these numbers is a significant landmark in the House investigation.

Until now, NIH officials said that the institutes and centers had no standard guidelines for reporting PR spending.

Indeed, the label "PR" can cover a broad range of activities. According to a definition by the Public Relations Society of America, PR is "a strategic communication process that builds mutually beneficial relationships between organizations and their publics," which can include health education, outreach, press relations, processing of petitions submitted under the Freedom of Information Act—and interaction with Congress.

The data provided to Congress haven't been seen—or compiled—before.

Responding to questions The Cancer Letter submitted under the FOIA earlier this year, NIH released only fragmentary data on five of its largest spenders on PR and health education (The Cancer Letter, March 1).

The Congressional investigators are focused on potential duplication and waste in these PR programs. The fact that the magnitude of NIH expenditures is so considerable likely bolsters the investigation.

In his letter, NIH Director Collins said his office and the institutes are working to contain PR and education costs.

"Two examples of this collaborative work are in the areas of: (1) developing decision-tree strategies for print vs. digital dissemination, and (2) collaboration on clinical trials information and recruitment announcements in a shared location," he wrote in the letter dated June 24.

The probe represents an unusual challenge for NIH and NCI, as no one seems to be able to remember the last time the appropriations and authorizing committees collaborated on a probe.

While appropriators control the purse strings, the authorizing committee has the power to legislate.

In fact, over half a century or so, the committee had a hand in inserting every single one of the 55 PHS Act mandates Collins mentions in his response. By the same token, the committee has the power to start yanking those mandates, either one-by-one or altogether. The NIH response can serve as a blueprint for such housecleaning.

A spokesman for the Committee on Energy and Commerce acknowledged that the letter from Collins has been received.

NIH IC	Total IC Appropriations FY 2012[1]	IC Communications Budget FY 2012[1]	Communications Budget as Percent of Overall IC Budget
NCI	$5,072,183,421	$46,186,000	0.911%
NIAID	$4,490,711,484	$7,254,286	0.162%
NHLBI	$3,079,020,632	$10,076,000	0.327%
NIGMS	$2,430,035,536	$2,285,435	0.094%
NIDDK	$1,947,044,155[2]	$11,847,191	0.608%
NINDS	$1,626,365,349	$5,491,044	0.338%
NIMH	$1,480,265,001	$6,559,455	0.443%
OD-OCPL	$1,459,117,047	$7,331,980	0.502%
Other OD Program Offices[3]	$1,459,117,047	$14,458,272	0.991%
NICHD	$1,321,397,829	$5,422,849	0.410%
NIA	$1,103,440,548	$5,366,490	0.486%
NIDA	$1,053,367,366	$9,313,586	0.884%
NIEHS	$764,498,332	$10,238,473	1.339%
NEI	$702,712,359	$6,764,502	0.963%
NCATS	$575,366,498	$3,175,874	0.552%
NIAMS	$535,786,446	$4,483,594	0.837%
NHGRI	$512,872,835	$2,950,000	0.575%
NIAAA	$459,518,865	$4,243,500	0.923%
NIDCD	$416,272,755	$2,729,000	0.656%
NIDCR	$410,710,288	$2,507,984	0.611%
NIBIB	$338,357,294	$1,360,854	0.402%
NLM	$337,638,655	$3,551,000	1.052%
NIMHD	$276,439,540	$666,000	0.241%
NINR	$144,768,869	$1,265,000	0.874%
NCCAM	$128,056,515	$5,113,043	3.993%
FIC	$69,622,165	$619,643	0.890%
Total NIH budget	$30,860,913,436[4,5]	$181,261,055	0.587%*

*Communications budgets across the NIH ICs represent less than one percent of the total NIH IC appropriations (FY 2012).

Notes on this table:

1) This column's individual components do not sum to the 'Total NIH budget' due to the nature of both centrally funded initiatives and offices at the NIH, as well as notes #3 and #4.
2) Includes $150 million from the Special Statutory Funding Program for Type 1 Diabetes Research. This appropriation is administered by the NIDDK on behalf of the HHS Secretary. These funds are separate from the regular appropriation and are dedicated to pursuing research on type 1 diabetes.
3) 'Other OD Program Offices' include the following OD offices: OIR, OER, ORS-ORF, and DPCPSI.
4) CSR, CC, and CIT are not included in this table, as they are funded through trans-NIH mechanisms.
5) While not a separate line on the table, the overall total appropriated dollars of $30.86 billion includes $125,343,652 in funds for the NIH Buildings and Facilities program (B&F), which supports the design and construction of new facilities for the NIH and the continuing repair and improvement of existing facilities.

Source: NIH

"The committee staff is reviewing and analyzing the information provided by NIH," the spokesman said.

House Democrats aren't a part of the investigation.

The investigation creates a dilemma for advocates who lobby for increased funding for NIH.

The journal Nature, in a recent editorial, said that NCI's spending on PR and education was excessive.

The Federation of American Societies for Experimental Biology apparently had to choose between its roles of advocating for NIH funding and its role of speaking for scientists who are frustrated by dropping success rates at NIH and who stand to benefit from redirecting of funds to research.

Recently, FASEB had a letter published in Nature, arguing that advocating for overall funding for science should take precedence over squabbles over what amounts to a small proportion of the budget.

NCI Cutting OCE Budget

The shrinking of the budget, combined with questions from Congressional investigators, and—perhaps most importantly—his stated intent to free up money for research, have prompted NCI Director Harold Varmus to scale back the budget of the Office of Communication and Education, which conducts most of the PR and education work in cancer.

Varmus has cut the OCE budget by about 15 percent so far this year, as part of his response to sequestration, and he apparently expects to slash another 15 percent in fiscal 2014.

"We are at a point now where we are going to be settling institute at that new level," Lenora Johnson, director of OCE, said to an ad hoc subcommittee of NCAB recently. "We are looking at a level that is hovering around $30 million.

"That has resulted in an immediate scurry to try to accommodate reductions of that significance, and so we have been going through the process of reassigning staff members to other areas of NCI."

Johnson said that on May 20, she and Varmus met with Congressional investigators Alan Slobodin, the Republican chief investigative counsel for oversight and investigations, and John Bartrum, an appropriations staff member.

"I accompanied [Varmus] to brief both of these individuals specifically about the similar issues about OCE NCI," Johnson said at the NCAB subcommittee meeting June 23. "We spent about an hour with them, responding to questions about budget and spending and activities with regard to my office."

It's not clear how much money will be saved as a result of these reassignments, as NCI isn't reducing its workforce, and—unlike the Department of Defense—not resorting to furloughs to shoehorn spending into the sequestration levels.

If OCE staff members are simply shifted to other parts of the institute, little or no money would be saved.

Having made many of the cuts at OCE, Varmus has narrowed the focus of advice he sought from the NCAB subcommittee NCI convened late last year to revamp its communications (The Cancer Letter, Dec. 7, 2012).

Instead of asking for broad strategic advice, Varmus is now asking the subcommittee to examine "NCI's public-facing web presences and operations and the levels of variations in web-related communications and content/data dissemination activities aimed at providing information to various audiences."

The committee is being asked to develop a report analyzing "how NCI's web presence aligns with, or diverges from, industry best practices as well as how NCI's efforts might be better coordinated, resourced, managed, and made more efficient."

This narrow charge surprised some committee members, who are experts in public health, health communications, basic science and the practice of

The Cancer Letter Series on the Cost of Cancer Communications

- **Dec. 7, 2012:** "Is $45 Million Too Much to Spend on PR? NCAB Panel Weighs NCI Communications Budget"
- **Feb. 1:** "NCI Ends Brash Foray Into the News Business—Emails Tell the Story of the NCI Cancer Bulletin"
- **March 1:** "NCI Spent $381.2 Million on PR from 2006 to 2012, Vastly Outspending Other NIH, FDA Units"
- **March 15:** "Nature Editorial Criticizes NCI PR spending"
- **June 14:** "FASEB: Focus on Research Funding, Not PR"

Monthly Visits Share

Rank	Websites (8 returned)	Total Visits	Visits Share ▼	Rank Apr 13	Rank Mar 13	Rank Feb 13
1	American Cancer Society	3,026,878	47.76%	1	1	2
▲ 2	National Cancer Institute	1,257,130	19.84%	3	3	3
▼ 3	Cancer Treatment Centers of A...	1,136,376	17.93%	2	2	1
4	About Cancer	340,920	5.38%	4	4	4
5	Cancer.net	231,871	3.66%	5	5	5
6	CancerCompass	227,826	3.59%	6	6	6
7	Live Strong	72,548	1.14%	7	7	7
8	Cancer Care	44,339	0.70%	8	8	8

Source: NCI Office of Communications and Education, based on data from Experian Hitwise

How NCI's web analytics compare to those of other organizations that provide cancer information.

oncology. "Could we get an appropriate consultant if we are going to really pursue this?" said Jonathan Samet, director of the University of Southern California Institute for Global Health and a member of NCAB.

Subcommittee members were in agreement that before addressing the question of best practices they needed to define the audience NCI should address.

"Our first priority, which will take a while to hash out, is whom this serves," said Victoria Champion, chair of the NCAB subcommittee, professor at the Department of Environments for Health and Associate Director of Population Science, Indiana University Simon Cancer Center.

Several committee members said there may no longer be a reason for NCI to communicate with the lay public.

"What should NCI be doing and what should it not be doing?" asked Kevin Cullen, director of the University of Maryland Greenebaum Cancer Center and a member of NCAB. "The problem we face right now is that NCI and [the American Cancer Society] and many other providers is they are trying to be all things for all people and you have an enormous amount of duplication at great expense to both ACS and NCI.

"It makes perfect sense to me that NCI serve the research community with communications around grants, shared data, data informatics. What makes less sense to me is whether NCI should be investing this much time and effort in information for the public, which is developed and promulgated by many other sources.

"It seems that before you move forward with a structure like this you have to take a step back and say what should our main focus be? At first pass it would seem that serving your academic community. Serving your researchers both with tools that permit them to function and share information would be a core thing. For other organizations it may be developing information for the lay public."

Cullen said he refers to three cancer information websites regularly.

"I use www.cancer.gov if I am dealing with research issues," Cullen said. "If I am dealing with cancer statistics, I use the ACS website. If I am directing patients to cancer information, I usually direct them to the ACS website. Another website that's valuable—it's a niche website—it's the NCCN guidelines. NCCN has spent an enormous amount of effort to developed evidence-based guidelines for treatment."

OCE Director Johnson said the institute is bound by Congressional mandates to provide information to patients.

"NCI has federal mandates—and some of them are quite explicit—as to what we are required to do," she said.

According to web statistics compiled by OCE, the institute is a distant number two to the American Cancer Society, and runs barely ahead of the Cancer Treatment Centers of America.

Between January and May, ACS logged over 3 million visits, NCI 1.26 million, and CTCA 1.14 million. The report is posted on The Cancer Letter website.

Collins Responds to Congressional Investigators

The text of Collins's respose to Congressional appropriations and authorizing committees follows:

Thank you for the opportunity to respond to questions related to the National Institutes of Health (NIH)'s communications and public education efforts. As you know, the NIH is the lead federal agency for supporting and conducting biomedical research in the

United States. An essential part of the NIH's mission is to translate and communicate research findings to patients and their families, health care providers, and the general public, with the ultimate goal of improving human health.

There is a long history of legislative mandates, authorities, and directives that charge the NIH and its Institutes and Centers (ICs) and the Office of the Director (OD) to carry out communications efforts. In fact, there are more than 55 provisions within the Public Health Service (PHS) Act that authorize the NIH to disseminate health information and conduct and support public education activities, such as clearinghouses, awareness programs, and public engagement efforts. Examples of congressional authorities are listed at the beginning of each of the enclosed individual IC sections.

The NIH communication and education programs, activities, and products provide patients, the general public, and health care professionals access to important health and science information from taxpayer-supported biomedical research.

Given that the NIH conducts and supports biomedical research on several hundred chronic diseases and thousands of rare diseases, our communication products are diverse and tailored to the particular disease or condition and each affected population.

The NIH also strives to respond to the ever-changing communication technology landscape by using a full array of print, electronic, web-based, and social media tools to reach patients, health care providers, and our other audiences.

While these communication efforts are robust and represent a major component of the NIH's mission, the Agency spends less than 1 percent of its budget on communication and education activities.

The NIH communication activities range from reporting the latest findings on specific health and science matters—such as cancer, infectious diseases, and diabetes—to raising awareness about health disparities and announcing groundbreaking scientific initiatives, such as the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) initiative.

Every week, there are hundreds of citations about NIH-conducted or -supported research in newspapers, magazines, on radio and television programs, websites, and all forms of social media.

The NIH plays an essential role in keeping the media and the public apprised of the progress of biomedical research and what it means in practical terms for patients and their families.

In addition to reporting breaking news, a number of the ICs carry out long-term communication programs on topics such as heart disease, neurological disorders, child and maternal health, arthritis, and substance abuse, to raise awareness that can translate into better public health. The number of NIH communication and education programs reflects the breadth, scope, and depth of the NIH research portfolio.

NIH leadership often hears from members of Congress, advocacy organizations, and scientific and public advisory committees that the public should be informed of the research advances made possible by the NIH and given easy access to health and science information.

This is especially important since the NIH provides unbiased, evidence-based health and medical information that is available free of charge.

As mentioned in your letter, with increasingly tight federal budgets, the need to find ways to control spending and work more efficiently has never been greater. The NIH recognizes this need and, over the past several years, the ICs and OD offices have increased their own internal communications and coordination, working strategically and collaboratively to share resources and lower costs.

Two examples of this collaborative work are in the areas of: (1) developing decision-tree strategies for print vs. digital dissemination, and (2) collaboration on clinical trials information and recruitment announcements in a shared location.

We have established a trans-NIH communications working group to evaluate shifting the balance of print versus digital formats for health information publications, which will result in savings on production and warehousing costs while serving audiences who have special needs or insufficient access to electronic formats.

Another example of a resource-saving collaboration is in the area of clinical research, vital to the agency's mission of enhancing human health, lengthening life, and reducing the burdens of illness.

Thanks to research advances, greater numbers of clinical trial volunteers are needed more than ever, but often studies are limited by under-recruitment.

The patient recruitment challenge has serious implications for the success or failure of research. Individual IC efforts aimed at expanding recruitment are described online: www.nih.gov/health/clinicaltrials/index.htm.

In addition, the OD's Office of Communications and Public Liaison leads a trans-NIH working group focused on the introduction to clinical research. The flagship website is http://www.nih.gov/health/clinicaltrials/index.htm, which complements the NIH's groundbreaking clinicaltrials.gov website. The newest addition to the effort is a centralized location for disease registries at www.nih.gov/health/clinicaltrials/registries.htm.

This collaboration continues to grow, meeting an important public need and promoting efficiency. In addition, the agency's ongoing collaboration with a grantee institution-sponsored service encourages broad access to high-quality information.

Thank you again for the opportunity to describe the NIH's communication and education activities. The NIH is a trusted source for millions of Americans, and communicating useful health and science information to the American public is central to our mission.

Please find enclosed a report from each IC as well as reports from the OD. Each report includes office descriptions and expenditures, including contracts. If you have any questions, please contact me or John Burklow, NIH Associate Director for Communications and Public Liaison.

Sincerely yours,

Francis S. Collins

NCI Section of Response to Congress

The text of the NCI section of the NIH response follows:

National Cancer Institute (NCI), Office of Communications and Education (OCE) and Office of Public Affairs and Research Communications (OPARC) IC Established 1937

Representative legislative language, provisions, and mandates that direct and shape the Institute's communications efforts:

Public Health Service Act 42 USC §285a-2 Special authorities of Director

(a) Information and education program

(1) The Director of the Institute shall establish an information and education program to collect, identify, analyze, and disseminate on a timely basis, through publications and other appropriate means, to cancer patients and their families, physicians and other health professionals, and the general public, information on cancer research, diagnosis, prevention, and treatment (including information respecting nutrition programs for cancer patients and the relationship between nutrition and cancer).

The Director of the Institute may take such action as may be necessary to insure that all channels for the dissemination and exchange of scientific knowledge and information are maintained between the Institute and the public and between the Institute and other scientific, medical, and biomedical disciplines and organizations nationally and internationally.

(2) In carrying out paragraph (1), the Director of the Institute shall-

(A) provide public and patient information and education programs, providing information that will help individuals take personal steps to reduce their risk of cancer, to make them aware of early detection techniques and to motivate appropriate utilization of those techniques, to help individuals deal with cancer if it strikes, and to provide information to improve

long-term survival;

(B) continue and expand programs to provide physicians and the public with state-of-the-art information on the treatment of particular forms of cancers, and to identify those clinical trials that might benefit patients while advancing knowledge of cancer treatment;

(E) to the extent practicable, in disseminating the results of such cancer research and treatment, utilize information systems available to the public.

The National Cancer Institute is the nation's primary federal support for cancer research and training, dedicated to eliminating cancer-related suffering and death.

Specifically, the NCI is at the heart of advances made in the diagnosis and treatment of cancer, conducting programs that study causes, prevention, and cures while promoting rehabilitation and continuing care of cancer patients and their families. Through the communication and dissemination of basic, translational, and clinical research findings, the NCI changes clinical practice and stimulates further research.

Centralized communications activities for the NCI are carried out through the Office of Communications and Education (OCE) and the Office of Public Affairs and Research Communications (OPARC). The OCE develops and disseminates information and educational materials on cancer research to cancer patients and their caregivers, physicians and other health professionals, and the public.

The information is developed in various formats for a wide variety of audiences, utilizing web, print, online platforms, phone service, and strategic dissemination partnerships. The OPARC includes the NCI's Office of Media Relations, which responds to media inquiries and develops relationships with the Public Information Offices at grantee institutions.

Three significant programs within the OCE are the NCI's Cancer Information Service (CIS), the Physician's Data Query (PDQ), and the complete NCI digital media enterprise.

• The CIS provides up-to-date information for consumers on cancer diagnosis, treatment, risk factors, symptoms, early detection, and smoking cessation, among numerous other topics through a toll-free number as well as through LiveHelp, an online chat service. Trained information specialists provide the latest cancer research information to patients and their caregivers and offer available clinical trials, as appropriate.

• PDQ contains summaries on a wide range of cancer topics, levels of evidence for numerous treatments, and a registry of more than 8,000 open cancer clinical trials. PDQ evidence synthesizes summaries, which are separately written for health professionals and patients, and developed by independent editorial boards. The scientific divisions, offices and centers of the NCI also may have communications investments that support their specific scientific portfolio.

These investments support the communication of cancer research to specific audiences.

Research findings have limited value if they are not available to the people who can use them.

• The NCI's digital media products include cancer.gov, cancer.gov/espanol, m.cancer.gov, all of its social media platforms, a robust multi-channel YouTube platform, video and editing production, and mobile applications for mobile phones and tablets.

Separate from the contract costs listed below, the NCI's communications budget, including personnel costs, is as follows for FY 2010 - FY 2013:

	Communications Budget
FY 2010	$21,716,507
FY 2011	$19,717,195
FY 2012	$19,368,203
FY 2013	$15,347,141

During this period, the NCI has had communications contracts with the Fred Hutchinson Cancer Research Center, Lockheed Martin/Verizon, ICF, Vocus, Webfirst, Newswise, Eurekaalert, Critical Mention, Automatic Sync Tech, Sapient and Lockheed Martin, Vigilant, AED, UCD, Ogilvy, and Idox. These communications contracts total:

	Contracts
FY 2010	$29,384,493
FY 2011	$28,351,805
FY 2012	$26,817,797
FY 2013	$23,851,859

Turmoil in Texas

AVEO Receives SEC Subpoena

(Continued from page 1)

survival on the tivozanib arm in the company's trial would present a problem (The Cancer Letter, May 10).

DePinho, a member of the AVEO board at the time, said he didn't know about the content of the meeting with FDA and apologized for giving stock advice, stating that it was inconsistent with his role as a Texas state employee.

DePinho has since stepped off the AVEO board, but his wife Lynda Chin, a senior scientist at MD Anderson, continues to serve as a member of the AVEO scientific advisory board. In an earlier statement to The Cancer Letter, DePinho acknowledged that he has been selling his stocks, including AVEO. Since he is no longer an AVEO board members, such trades aren't publicly disclosed.

MD Anderson and DePinho declined to comment on the subpoena.

In recent weeks, AVEO has been the target of multiple shareholders' suits.

The company's stock, which was trading at $2.54 per share when the market closed July 11, dropped by 14 percent in after-hour trading after the news of the SEC probe hit. In May 2012, when DePinho appeared on CNBC, the company's stock hovered around $12 per share.

The text of AVEO's announcement follows:

"On July 3, 2013, AVEO Pharmaceuticals, Inc. (the "Company") received a subpoena from the United States Securities and Exchange Commission ("SEC") requesting documents and information concerning tivozanib, which the U.S. Food and Drug Administration ("FDA") declined to approve for the treatment of patients with advanced renal cell carcinoma on June 10, 2013, including related communications with the FDA, investors and others.

"The Company intends to fully cooperate with the SEC regarding this non-public, fact-finding inquiry. The SEC has informed the Company that this inquiry should not be construed as an indication that any violations of law have occurred or that the SEC has any negative opinion of any person, entity or security. The Company does not intend to comment further on this matter unless and until this matter is closed or further action is taken by the SEC, which, in the Company's judgment, merits further comment or public disclosure."

An updated tivozanib time line follows:

The Tivozanib Timeline

December 2009, 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 significantmprovement 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 12, 2012

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 OS showed a trend toward a detrimental effect on OS with tivozanib; HR=1.25, p=0.11. Median OS was 28.8 mos. in the tivozanib arm and 29.3 mos. in the sorafenib arm. See the FDA briefing documents for ODAC. The agency declined to release the exact date of the pre-NDA meeting, but sources in Houston say the meeting occurred on May 12, 2012.

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.

May 17, 2013

Astellas Pharma Inc., the Japanese partner of AVEO Oncology Inc., said it would not submit a European application for the drug tivozanib and would not sponsor any more clinical trials of the agent for renal cell carcinoma.

June 10, 2013

FDA declines to approve tivozanib, taking ODAC's advice.

July 11, 2013

Securities and Exchange Commission issues a subpoena requesting information on tivozanib.

Obituary

Gregory Foltz, Neurosurgeon At Swedish Medical Center

Gregory Foltz, founder and director of the Ben & Catherine Ivy Center for Advanced Brain Tumor Treatment at Swedish Medical Center, died June 27. He was 50 and had pancreatic cancer.

A career pianist at 22, Foltz was heading for study at The Juilliard School when a friend's daughter died from brain cancer.

He enrolled in the Washington University School of Medicine in St. Louis, graduated in 1995, and later became chief resident in neurological surgery at the University of Washington.

He was co-director of the neurogenomics research lab at the University of Iowa College of Medicine.

Since the Ivy Center's inception in 2008, Foltz raised nearly $14 million for brain cancer research.

As director, he established research collaborations and alliances among research and biotech institutions in the Pacific Northwest, including the Institute for Systems Biology, Allen Institute for Brain Science, and the Fred Hutchinson Cancer Research Center.

Foltz also helped create the Seattle Brain Cancer Walk in 2008 to raise funds.

The Walk has grown from raising $120,000 in its first year to raising nearly $1 million in 2012. This year's annual Walk will be held on Saturday, Sept. 21, 2013.

Foltz and his colleagues learned that brain cancer is highly variable from patient to patient and developed ways to test new treatments.

After mapping the genetics of each patient's tumor, his laboratory breeds mice with the tumor to test different drugs.

Foltz was born in Kansas City, Mo., and grew up in Rochester, Ill.

He is survived by his wife, Luba Foltz, two children, and parents, David Foltz and Shay Malcolm.

Donations may be made to the Greg Foltz, M.D., Endowed Directorship at the Ben & Catherine Ivy Center at Swedish Medical Center.